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(54) Title: CYTOCHROME P450 MONOOXYGENASE AND NADPH CYTOCHROME P450 OXIDOREDUCTASE GENES AND PROTEINS RELATED TO THE OMEGA HYDROXYLASE COMPLEX OF *CANDIDA TROPICALIS* AND METHODS RELATING THERETO

(57) Abstract

Novel genes have been isolated which encode cytochrome P450 and NADPH reductase enzyme of the ω-hydroxylase complex of *C. tropicalis* 20336. Vectors including these genes, transfected host cells and transformed host cells are provided. Methods of producing of cytochrome P450 and NADPH reductase enzymes are also provided which involve transforming a host cell with a gene encoding these enzymes and culturing the cells. Methods of increasing the production of a dicarboxylic acid and methods of increasing production of the aforementioned enzymes are also provided which involve increasing in the host cell the number of genes encoding these enzymes. A method for discriminating members of a gene family by quantifying the expression of genes is also provided.

CYTOCHROME P450 MONOOXYGENASE AND NADPH CYTOCHROME P450 OXIDOREDUCTASE GENES AND PROTEINS RELATED TO THE OMEGA HYDROXYLASE COMPLEX OF *CANDIDA TROPICALIS* AND METHODS RELATING THERETO

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Provisional Application Serial No. 60/103,099 filed October 5, 1998, and U.S. Provisional Application Serial No. 60/083,798 filed May 1, 1998.

BACKGROUND

1. Field of the Invention

The present invention relates to novel genes which encode enzymes of the ω-hydroxylase complex in yeast *Candida tropicalis* strains. In particular, the invention relates to novel genes encoding the cytochrome P450 and NADPH reductase enzymes of the ω-hydroxylase complex in yeast *Candida tropicalis*, and to a method of quantitating the expression of genes.

2. Description of the Related Art

Aliphatic dioic acids are versatile chemical intermediates useful as raw materials for the preparation of perfumes, polymers, adhesives and macrolid antibiotics. While several chemical routes to the synthesis of long-chain alpha, ω-dicarboxylic acids are available, the synthesis is not easy and most methods result in mixtures containing shorter chain lengths. As a result, extensive purification steps are necessary. While it is known that long-chain dioic acids can also be produced by microbial transformation of alkanes, fatty acids or esters thereof, chemical synthesis has remained the most commercially viable route, due to limitations with the current biological approaches.

Several strains of yeast are known to excrete alpha, ω-dicarboxylic acids as a byproduct when cultured on alkanes or fatty acids as the carbon source. In particular, yeast belonging to the Genus *Candida*, such as *C. albicans, C. cloacae, C. guillermondii, C. intermedia, C. lipolytica, C. maltosa, C. parapsilosis* and *C. zeylenoides* are known to produce

such dicarboxylic acids (*Agr. Biol. Chem.* 35: 2033-2042 (1971)). Also, various strains of *C. tropicalis* are known to produce dicarboxylic acids ranging in chain lengths from C_{11} through C_{18} (Okino et al., BM Lawrence, BD Mookherjee and BJ Willis (eds), in *Flavors and Fragrances: A World Perspective*. Proceedings of the 10th International Conference of Essential Oils, Flavors and Fragrances, Elsevier Science Publishers BV Amsterdam (1988)), and are the basis of several patents as reviewed by Bühler and Schindler, in *Aliphatic Hydrocarbons in Biotechnology*, H. J. Rehm and G. Reed (eds), Vol. 169, Verlag Chemie, Weinheim (1984).

Studies of the biochemical processes by which yeasts metabolize alkanes and fatty acids have revealed three types of oxidation reactions: α-oxidation of alkanes to alcohols, ω-oxidation of fatty acids to alpha, ω-dicarboxylic acids and the degradative β-oxidation of fatty acids to CO_2 and water. The first two types of oxidations are catalyzed by microsomal enzymes while the last type takes place in the peroxisomes. In *C. tropicalis,* the first step in the ω-oxidation pathway is catalyzed by a membrane-bound enzyme complex (ω-hydroxylase complex) including a cytochrome P450 monooxygenase and a NADPH cytochrome reductase. This hydroxylase complex is responsible for the primary oxidation of the terminal methyl group in alkanes and fatty acids (Gilewicz et al., *Can. J. Microbiol.* 25:201 (1979)). The genes which encode the cytochrome P450 and NADPH reductase components of the complex have previously been identified as P450ALK and P450RED respectively, and have also been cloned and sequenced (Sanglard et al., *Gene* 76:121-136 (1989)). P450ALK has also been designated P450ALK1. More recently, ALK genes have been designated by the symbol *CYP* and RED genes have been designated by the symbol *CPR*. See, e.g., Nelson, *Pharmacogenetics* 6(1):1-42 (1996), which is incorporated herein by reference. See also Ohkuma et al., *DNA and Cell Biology* 14:163-173 (1995), Seghezzi et al., *DNA and Cell Biology*, 11:767-780 (1992) and Kargel et al., *Yeast* 12:333-348 (1996), each incorporated herein by reference. For example, P450ALK is also designated *CYP52* according to the nomenclature of Nelson, *supra*. Fatty acids are ultimately formed from alkanes after two additional oxidation steps, catalyzed by alcohol oxidase (Kemp et al., *Appl. Microbiol. and Biotechnol.* 28: 370-374 (1988)) and aldehyde dehydrogenase. The fatty acids can be further oxidized through the same or similar pathway to the corresponding dicarboxylic acid. The ω-oxidation of fatty acids proceeds via the ω-hydroxy fatty acid and its aldehyde derivative, to the corresponding dicarboxylic acid without the requirement for CoA activation. However, both fatty acids and dicarboxylic acids can be

degraded, after activation to the corresponding acyl-CoA ester through the β-oxidation pathway in the peroxisomes, leading to chain shortening. In mammalian systems, both fatty acid and dicarboxylic acid products of ω-oxidation are activated to their CoA-esters at equal rates and are substrates for both mitochondrial and peroxisomal β-oxidation (*J. Biochem.*, 102:225-234 (1987)). In yeast, β-oxidation takes place solely in the peroxisomes (*Agr.Biol.Chem.* 49:1821-1828 (1985)).

The production of dicarboxylic acids by fermentation of unsaturated C_{14}-C_{16} monocarboxylic acids using a strain of the species *C. tropicalis* is disclosed in U.S. Patent 4,474,882. The unsaturated dicarboxylic acids correspond to the starting materials in the number and position of the double bonds. Similar processes in which other special microorganisms are used are described in U.S. Patents 3,975,234 and 4,339,536, in British Patent Specification 1,405,026 and in German Patent Publications 21 64 626, 28 53 847, 29 37 292, 29 51 177, and 21 40 133.

Cytochromes P450 (P450s) are terminal monooxidases of a multicomponent enzyme system as described above. They comprise a superfamily of proteins which exist widely in nature having been isolated from a variety of organisms as described e.g., in Nelson, *supra*. These organisms include various mammals, fish, invertebrates, plants, mollusk, crustaceans, lower eukaryotes and bacteria (Nelson, *supra)*. First discovered in rodent liver microsomes as a carbon-monoxide binding pigment as described, e.g., in Garfinkel, *Arch. Biochem. Biophys*. 77:493-509 (1958), which is incorporated herein by reference, P450s were later named based on their
absorption at 450 nm in a reduced-CO coupled difference spectrum as described, e.g., in Omura et al., *J. Biol. Chem*. 239:2370-2378 (1964), which is incorporated herein by reference.

P450s catalyze the metabolism of a variety of endogenous and exogenous compounds (Nelson, *supra*). Endogenous compounds include steroids, prostanoids, eicosanoids, fat-soluble vitamins, fatty acids, mammalian alkaloids, leukotrines, biogenic amines and phytolexins (Nelson, *supra*). P450 metabolism involves such reactions as epoxidation, hydroxylation, deakylation, N-hydroxylation, sulfoxidation, desulfuration and reductive dehalogenation. These reactions generally make the compound more water soluble, which is conducive for excretion, and more electrophilic. These electrophilic products can have detrimental effects if they react with DNA or other cellular constituents. However, they can react

through conjugation with low molecular weight hydrophilic substances resulting in glucoronidation, sulfation, acetylation, amino acid conjugation or glutathione conjugation typically leading to inactivation and elimination as described, e.g., in Klaassen et al., *Toxicology*, 3rd ed, Macmillan, New York, 1986, incorporated herein by reference.

P450s are heme thiolate proteins consisting of a heme moiety bound to a single polypeptide chain of 45,000 to 55,000 Da. The iron of the heme prosthetic group is located at the center of a protoporphyrin ring. Four ligands of the heme iron can be attributed to the porphyrin ring. The fifth ligand is a thiolate anion from a cysteinyl residue of the polypeptide. The sixth ligand is probably a hydroxyl group from an amino acid residue, or a moiety with a similar field strength such as a water molecule as described, e.g., in Goeptar et al., *Critical Reviews in Toxicology* 25(1):25-65 (1995), incorporated herein by reference.

Monooxygenation reactions catalyzed by cytochromes P450 in a eukaryotic membrane-bound system require the transfer of electrons from NADPH to P450 via NADPH-cytochrome P450 reductase (*CPR*) as described, e.g., in Taniguchi et al., *Arch. Biochem. Biophys.* 232:585 (1984), incorporated herein by reference. *CPR* is a flavoprotein of approximately 78,000 Da containing 1 mol of flavin adenine dinucleotide (FAD) and 1 mol of flavin mononucleotide (FMN) per mole of enzyme as described, e.g., in Potter et al., *J. Biol. Chem.* 258:6906 (1983), incorporated herein by reference. The FAD moiety of *CPR* is the site of electron entry into the enzyme, whereas FMN is the electron-donating site to P450 as described, e.g., in Vermilion et al., *J. Biol. Chem.* 253:8812 (1978), incorporated herein by reference. The overall reaction is as follows:

$$H^+ + RH + NADPH + O_2 \rightarrow ROH + NADP^+ + H_2O$$

Binding of a substrate to the catalytic site of P450 apparently results in a conformational change initiating electron transfer from *CPR* to P450. Subsequent to the transfer of the first electron, O_2 binds to the Fe_2^+-P450 substrate complex to form Fe_3^+ -P450-substrate complex. This complex is then reduced by a second electron from *CPR*, or, in some cases, NADH via cytochrome b5 and NADH-cytochrome b5 reductase as described, e.g., in Guengerich et al., *Arch. Biochem. Biophys.* 205:365 (1980), incorporated herein by reference. One atom of this reactive oxygen is introduced into the substrate, while the other is reduced to water. The

oxygenated substrate then dissociates, regenerating the oxidized form of the cytochrome P450 as described, e.g., in Klassen, Amdur and Doull, *Casarett and Doull's Toxicology*, Macmillan, New York (1986), incorporated herein by reference.

The P450 reaction cycle can be short-circuited in such a way that O_2 is reduced to O_2^- and/or H_2O_2 instead of being utilized for substrate oxygenation. This side reaction is often referred to as the "uncoupling" of cytochrome P450 as described, e.g., in Kuthen et al., *Eur. J. Biochem.* 126:583 (1982) and Poulos et al., *FASEB* J. 6:674 (1992), both of which are incorporated herein by reference. The formation of these oxygen radicals may lead to oxidative cell damage as described, e.g., in Mukhopadhyay, *J. Biol. Chem.* 269(18):13390-13397 (1994) and Ross et al., *Biochem. Pharm.* 49(7):979-989 (1995), both of which are incorporated herein by reference. It has been proposed that cytochrome b5's effect on P450 binding to the *CPR* results in a more stable complex which is less likely to become "uncoupled" as described, e.g., in Yamazaki et al., *Arch. Biochem. Biophys.* 325(2):174-182 (1996), incorporated herein by reference.

P450 families are assigned based upon protein sequence comparisons. Notwithstanding a certain amount of heterogeneity, a practical classification of P450s into families can be obtained based on deduced amino acid sequence similarity. P450s with amino acid sequence similarity of between about 40 - 80% are considered to be in the same family, with sequences of about > 55% belonging to the same subfamily. Those with sequence similarity of about < 40% are generally listed as members of different P450 gene families (Nelson, *supra*). A value of about > 97% is taken to indicate allelic variants of the same gene, unless proven otherwise based on catalytic activity, sequence divergence in non-translated regions of the gene sequence, or chromosomal mapping.

The most highly conserved region is the HR2 consensus containing the invariant cysteine residue near the carboxyl terminus which is required for heme binding as described, e.g., in Gotoh et al. *J. Biochem.* 93:807-817 (1983) and Motohashi et al., *J. Biochem.* 101:879-997 (1987), both of which are incorporated herein by reference. Additional consensus regions, including the central region of helix I and the transmembrane region, have also been identified, as described, e.g, in Goeptar et al., *supra* and Kalb et al., *PNAS.* 85:7221-7225 (1988), incorporated herein by reference, although the HR2 cysteine is the only invariant amino acid among P450s.

Short chain (≤C12) aliphatic dicarboxylic acids (diacids) are important industrial intermediates in the manufacture of diesters and polymers, and find application as thermoplastics, plasticizing agents, lubricants, hydraulic fluids, agricultural chemicals, pharmaceuticals, dyes, surfactants, and adhesives. The high price and limited availability of short chain diacids are due to constraints imposed by the existing chemical synthesis.

Long-chain diacids (aliphatic α, ω-dicarboxylic acids with carbon numbers of 12 or greater, hereafter also referred to as diacids) ($HOOC-(CH_2)_n-COOH$) are a versatile family of chemicals with demonstrated and potential utility in a variety of chemical products including plastics, adhesives, and fragrances. Unfortunately, the full market potential of diacids has not been realized because chemical processes produce only a limited range of these materials at a relatively high price. In addition, chemical processes for the production of diacids have a number of limitations and disadvantages. All the chemical processes are restricted to the production of diacids of specific carbon chain lengths. For example, the dodecanedioic acid process starts with butadiene. The resulting product diacids are limited to multiples of four-carbon lengths and, in practice, only dodecanedioic acid is made. The dodecanedioic process is based on nonrenewable petrochemical feedstocks. The multireaction conversion process produces unwanted byproducts, which result in yield losses, NO_x pollution and heavy metal wastes.

Long-chain diacids offer potential advantages over shorter chain diacids, but their high selling price and limited commercial availability prevent widespread growth in many of these applications. Biocatalysis offers an innovative way to overcome these limitations with a process that produces a wide range of diacid products from renewable feedstocks. However, there is no commercially viable bioprocess to produce long chain diacids from renewable resources.

SUMMARY OF THE INVENTION

An isolated nucleic acid is provided which encodes a *CPRA* protein having the amino acid sequence set forth in SEQ ID NO: 83. An isolated nucleic acid is also provided which includes a coding region defined by nucleotides 1006-3042 as set forth in SEQ ID NO: 81. An isolated protein is provided which includes an amino acid sequence as set forth in SEQ ID NO: 83. A vector is provided which includes a nucleotide sequence encoding *CPRA* protein

including an amino acid sequence as set forth in SEQ ID NO: 83. A host cell is provided which is transfected or transformed with the nucleic acid encoding *CPRA* protein having an amino acid sequence as set forth in SEQ ID NO: 83. A method of producing a *CPRA* protein including an amino acid sequence as set forth in SEQ ID NO: 83 is also provided which includes a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 83; and b) culturing the cell under conditions favoring the expression of the protein.

An isolated nucleic acid is provided which encodes a *CPRB* protein having the amino acid sequence set forth in SEQ ID NO: 84. An isolated nucleic acid is provided which includes a coding region defined by nucleotides 1033-3069 as set forth in SEQ ID NO: 82. An isolated protein is provided which includes an amino acid sequence as set forth in SEQ ID NO: 84. A vector is provided which includes a nucleotide sequence encoding *CPRB* protein including an amino acid sequence as set forth in SEQ ID NO: 84. A host cell is provided which is transfected or transformed with the nucleic acid encoding *CPRB* protein having an amino acid sequence as set forth in SEQ ID NO: 84. A method of producing a *CPRB* protein including an amino acid sequence as set forth in SEQ ID NO: 84 is provided which includes a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 84; and b) culturing the cell under conditions favoring the expression of the protein.

An isolated nucleic acid is provided which encodes a *CYP52A1A* protein having the amino acid sequence set forth in SEQ ID NO: 95. An isolated nucleic acid is provided which includes a coding region defined by nucleotides 1177-2748 as set forth in SEQ ID NO: 85. An isolated protein is provided which includes an amino acid sequence as set forth in SEQ ID NO: 95. A vector is provided which includes a nucleotide sequence encoding *CYP52A1A* protein including an amino acid sequence as set forth in SEQ ID NO: 95. A host cell is provided which is transfected or transformed with the nucleic acid encoding *CYP52A1A* protein having an amino acid sequence as set forth in SEQ ID NO: 95. A method of producing a *CYP52A1A* protein including an amino acid sequence as set forth in SEQ ID NO: 95 is provided which includes a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 95; and b) culturing the cell under conditions favoring the expression of the protein.

An isolated nucleic acid encoding a *CYP52A2A* protein is provided which has the amino acid sequence set forth in SEQ ID NO: 96. An isolated nucleic acid is provided which includes a coding region defined by nucleotides 1199-2767 as set forth in SEQ ID NO: 86. An isolated protein is provided which includes an amino acid sequence as set forth in SEQ ID NO: 96. A vector is provided which includes a nucleotide sequence encoding *CYP52A2A* protein including an amino acid sequence as set forth in SEQ ID NO: 96. A host cell is provided which is transfected or transformed with the nucleic acid encoding *CYP52A2A* protein having an amino acid sequence as set forth in SEQ ID NO: 96. A method of producing a *CYP52A2A* protein including an amino acid sequence as set forth in SEQ ID NO: 96 is provided which includes a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 96; and b) culturing the cell under conditions favoring the expression of the protein.

An isolated nucleic acid encoding a *CYP52A2B* protein is provided which has the amino acid sequence set forth in SEQ ID NO: 97. An isolated nucleic acid is provided which includes a coding region defined by nucleotides 1072-2640 as set forth in SEQ ID NO: 87. An isolated protein is provided which includes an amino acid sequence as set forth in SEQ ID NO: 97. A vector is provided which includes a nucleotide sequence encoding *CYP52A2B* protein including an amino acid sequence as set forth in SEQ ID NO: 97. A host cell is provided which is transfected or transformed with the nucleic acid encoding *CYP52A2B* protein having an amino acid sequence as set forth in SEQ ID NO: 97. A method of producing a *CYP52A2B* protein including an amino acid sequence as set forth in SEQ ID NO: 97 is provided which includes a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 97; and b) culturing the cell under conditions favoring the expression of the protein.

An isolated nucleic acid encoding a *CYP52A3A* protein is provided which has the amino acid sequence set forth in SEQ ID NO: 98. An isolated nucleic acid is provided which includes a coding region defined by nucleotides 1126-2748 as set forth in SEQ ID NO: 88. An isolated protein is provided which includes an amino acid sequence as set forth in SEQ ID NO: 98. A vector is provided which includes a nucleotide sequence encoding *CYP52A3A* protein including an amino acid sequence as set forth in SEQ ID NO: 98. A host cell is provided which is transfected or transformed with the nucleic acid encoding *CYP52A3A* protein having an

amino acid sequence as set forth in SEQ ID NO: 98. A method of producing a *CYP52A3A* protein including an amino acid sequence as set forth in SEQ ID NO: 98 is provided which includes a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 98; and b) culturing the cell under conditions favoring the expression of the protein.

An isolated nucleic acid encoding a *CYP52A3B* protein is provided having the amino acid sequence as set forth in SEQ ID NO: 99. An isolated nucleic acid is provided which includes a coding region defined by nucleotides 913-2535 as set forth in SEQ ID NO: 89. An isolated protein is provided which includes an amino acid sequence as set forth in SEQ ID NO: 99. A vector is provided which includes a nucleotide sequence encoding *CYP52A3B* protein including an amino acid sequence as set forth in SEQ ID NO: 99. A host cell is provided which is transfected or transformed with the nucleic acid encoding *CYP52A3B* protein having an amino acid sequence as set forth in SEQ ID NO: 99. A method of producing a *CYP52A3B* protein including an amino acid sequence as set forth in SEQ ID NO: 99 is provided which includes a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 99; and b) culturing the cell under conditions favoring the expression of the protein.

An isolated nucleic acid encoding a *CYP52A5A* protein is provided having the amino acid sequence set forth in SEQ ID NO: 100. An isolated nucleic acid is provided which includes a coding region defined by nucleotides 1103-2656 as set forth in SEQ ID NO: 90. An isolated protein is provided which includes an amino acid sequence as set forth in SEQ ID NO: 100. A vector is provided which includes a nucleotide sequence encoding *CYP52A5A* protein including an amino acid sequence as set forth in SEQ ID NO: 100. A host cell is provided which is transfected or transformed with the nucleic acid encoding *CYP52A5A* protein having an amino acid sequence as set forth in SEQ ID NO: 100. A method of producing a *CYP52A5A* protein including an amino acid sequence as set forth in SEQ ID NO: 100 is provided which includes a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 100; and b) culturing the cell under conditions favoring the expression of the protein.

An isolated nucleic acid encoding a *CYP52A5B* protein is provided having the amino acid sequence as set forth in SEQ ID NO: 101. An isolated nucleic acid is provided

which includes a coding region defined by nucleotides 1142-2695 as set forth in SEQ ID NO: 91. An isolated protein is provided which includes an amino acid sequence as set forth in SEQ ID NO: 101. A vector is provided which includes a nucleotide sequence encoding *CYP52A5B* protein including the amino acid sequence as set forth in SEQ ID NO: 101. A host cell is provided which is transfected or transformed with the nucleic acid encoding *CYP52A5B* protein having the amino acid sequence as set forth in SEQ ID NO: 101. A method of producing a *CYP52A5B* protein including an amino acid sequence as set forth in SEQ ID NO: 101 is provided which includes a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 101; and b) culturing the cell under conditions favoring the expression of the protein.

An isolated nucleic acid encoding a *CYP52A8A* protein is provided having the amino acid sequence set forth in SEQ ID NO: 102. An isolated nucleic acid is provided which includes a coding region defined by nucleotides 464-2002 as set forth in SEQ ID NO: 92. An isolated protein is provided which includes an amino acid sequence as set forth in SEQ ID NO: 102. A vector is provided which includes a nucleotide sequence encoding *CYP52A8A* protein including an amino acid sequence as set forth in SEQ ID NO: 102. A host cell is provided which is transfected or transformed with the nucleic acid encoding *CYP52A8A* protein having an amino acid sequence as set forth in SEQ ID NO: 102. A method of producing a *CYP52A8A* protein including an amino acid sequence as set forth in SEQ ID NO: 102 is provided which includes a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 102; and b) culturing the cell under conditions favoring the expression of the protein.

An isolated nucleic acid encoding a *CYP52A8B* protein is provided having the amino acid sequence set forth in SEQ ID NO: 103. An isolated nucleic acid is provided which includes a coding region defined by nucleotides 1017-2555 as set forth in SEQ ID NO: 93. An isolated protein is provided which includes an amino acid sequence as set forth in SEQ ID NO: 103. A vector is provided which includes a nucleotide sequence encoding *CYP52A8B* protein including an amino acid sequence as set forth in SEQ ID NO: 103. A host cell is provided which is transfected or transformed with the nucleic acid encoding *CYP52A8B* protein having an amino acid sequence as set forth in SEQ ID NO: 103. A method of producing a *CYP52A8B* protein including an amino acid sequence as set forth in SEQ ID NO: 103 is provided which

includes a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 103; and b) culturing the cell under conditions favoring the expression of the protein.

An isolated nucleic acid encoding a *CYP52D4A* protein is provided having the amino acid sequence set forth in SEQ ID NO: 104. An isolated nucleic acid is provided including a coding region defined by nucleotides 767-2266 as set forth in SEQ ID NO: 94. An isolated protein is provided which includes an amino acid sequence as set forth in SEQ ID NO: 104. A vector is provided which includes a nucleotide sequence encoding *CYP52D4A* protein including an amino acid sequence as set forth in SEQ ID NO: 104. A host cell is provided which is transfected or transformed with the nucleic acid encoding *CYP52D4A* protein having an amino acid sequence as set forth in SEQ ID NO: 104. A method of producing a *CYP52D4A* protein including an amino acid sequence as set forth in SEQ ID NO: 104 is provided which includes a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 104; and b) culturing the cell under conditions favoring the expression of the protein.

A method for discriminating members of a gene family by quantifying the amount of target mRNA in a sample is provided which includes a) providing an organism containing a target gene; b) culturing the organism with an organic substrate which causes upregulation in the activity of the target gene; c) obtaining a sample of total RNA from the organism at a first point in time; d) combining at least a portion of the sample of the total RNA with a known amount of competitor RNA to form an RNA mixture, wherein the competitor RNA is substantially similar to the target mRNA but has a lesser number of nucleotides compared to the target mRNA; e) adding reverse transcriptase to the RNA mixture in a quantity sufficient to form corresponding target DNA and competitor DNA; (f) conducting a polymerase chain reaction in the presence of at least one primer specific for at least one substantially non-homologous region of the target DNA within the gene family, the primer also specific for the competitor DNA; g) repeating steps (c-f) using increasing amounts of the competitor RNA while maintaining a substantially constant amount of target RNA; h) determining the point at which the amount of target DNA is substantially equal to the amount of competitor DNA; i) quantifying the results by comparing the ratio of the concentration of unknown target to the known concentration of competitor; and j)

obtaining a sample of total RNA from the organism at another point in time and repeating steps (d-i).

A method for increasing production of a dicarboxylic acid is provided which includes a) providing a host cell having a naturally occurring number of *CPRA* genes; b) increasing, in the host cell, the number of *CPRA* genes which encode a *CPRA* protein having the amino acid sequence as set forth in SEQ ID NO: 83; c) culturing the host cell in media containing an organic substrate which upregulates the *CPRA* gene, to effect increased production of dicarboxylic acid.

A method for increasing the production of a *CPRA* protein having an amino acid sequence as set forth in SEQ ID NO: 83 is provided which includes a) transforming a host cell having a naturally occurring amount of *CPRA* protein with an increased copy number of a *CPRA* gene that encodes the *CPRA* protein having the amino acid sequence as set forth in SEQ ID NO: 83; and b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CPRA* gene.

A method for increasing production of a dicarboxylic acid is provided which includes a) providing a host cell having a naturally occurring number of *CPRB* genes; b) increasing, in the host cell, the number of *CPRB* genes which encode a *CPRB* protein having the amino acid sequence as set forth in SEQ ID NO: 84; c) culturing the host cell in media containing an organic substrate which upregulates the *CPRB* gene, to effect increased production of dicarboxylic acid.

A method for increasing the production of a *CPRB* protein having an amino acid sequence as set forth in SEQ ID NO: 84 is provided which includes a) transforming a host cell having a naturally occurring amount of *CPRB* protein with an increased copy number of a *CPRB* gene that encodes the *CPRB* protein having the amino acid sequence as set forth in SEQ ID NO: 84; and b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CPRB* gene.

A method for increasing production of a dicarboxylic acid is provided which includes a) providing a host cell having a naturally occurring number of *CYP52A1A* genes; b) increasing, in the host cell, the number of *CYP52A1A* genes which encode a *CYP52A1A* protein having the amino acid sequence as set forth in SEQ ID NO: 95; c) culturing the host cell in media

containing an organic substrate which upregulates the *CYP52A1A* gene, to effect increased production of dicarboxylic acid.

A method for increasing the production of a *CYP52A1A* protein having an amino acid sequence as set forth in SEQ ID NO: 95 is provided which includes a) transforming a host cell having a naturally occurring amount of *CYP52A1A* protein with an increased copy number of a *CYP52A1A* gene that encodes the *CYP52A1A* protein having the amino acid sequence as set forth in SEQ ID NO: 95; and b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A1A* gene.

A method for increasing production of a dicarboxylic acid is provided which includes a) providing a host cell having a naturally occurring number of *CYP52A2A* genes; b) increasing, in the host cell, the number of *CYP52A2A* genes which encode a *CYP52A2A* protein having the amino acid sequence as set forth in SEQ ID NO: 96; c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A2A* gene, to effect increased production of dicarboxylic acid.

A method for increasing the production of a *CYP52A2A* protein having an amino acid sequence as set forth in SEQ ID NO: 96 is provided which includes a) transforming a host cell having a naturally occurring amount of *CYP52A2A* protein with an increased copy number of a *CYP52A2A* gene that encodes the *CYP52A2A* protein having the amino acid sequence as set forth in SEQ ID NO: 96; and b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A2A* gene.

A method for increasing production of a dicarboxylic acid is provided which includes a) providing a host cell having a naturally occurring number of *CYP52A2B* genes; b) increasing, in the host cell, the number of *CYP52A2B* genes which encode a *CYP52A2B* protein having the amino acid sequence as set forth in SEQ ID NO: 97; c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A2B* gene, to effect increased production of dicarboxylic acid.

A method for increasing the production of a *CYP52A2B* protein having an amino acid sequence as set forth in SEQ ID NO: 97 is provided which includes a) transforming a host cell having a naturally occurring amount of *CYP52A2B* protein with an increased copy number of

a *CYP52A2B* gene that encodes the *CYP52A2B* protein having the amino acid sequence as set forth in SEQ ID NO: 97; and b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A2B* gene.

A method for increasing production of a dicarboxylic acid is provided which includes a) providing a host cell having a naturally occurring number of *CYP52A3A* genes; b) increasing, in the host cell, the number of *CYP52A3A* genes which encode a *CYP52A3A* protein having the amino acid sequence as set forth in SEQ ID NO: 98; c) culturing the host cell in media containing an organic substrate which upregulates *CYP52A3A* gene, to effect increased production of dicarboxylic acid.

A method for increasing the production of a *CYP52A3A* protein having an amino acid sequence as set forth in SEQ ID NO: 98 is provided which includes a) transforming a host cell having a naturally occurring amount of *CYP52A3A* protein with an increased copy number of a *CYP52A3A* gene that encodes the *CYP52A3A* protein having the amino acid sequence as set forth in SEQ ID NO: 98; and b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A3A* gene.

A method for increasing production of a dicarboxylic acid is provided which includes a) providing a host cell having a naturally occurring number of *CYP52A3B* genes; b) increasing, in the host cell, the number of *CYP52A3B* genes which encode a *CYP52A3B* protein having the amino acid sequence as set forth in SEQ ID NO: 99; c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A3B* gene, to effect increased production of dicarboxylic acid.

A method for increasing the production of a *CYP52A3B* protein having an amino acid sequence as set forth in SEQ ID NO: 99 is provided which includes a) transforming a host cell having a naturally occurring amount of *CYP52A3B* protein with an increased copy number of a *CYP52A3B* gene that encodes the *CYP52A3B* protein having the amino acid sequence as set forth in SEQ ID NO: 99; and b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A3B* gene.

A method for increasing production of a dicarboxylic acid is provided which includes a) providing a host cell having a naturally occurring number of *CYP52A5A* genes; b) increasing, in the host cell, the number of *CYP52A5A* genes which encode a *CYP52A5A* protein having the amino acid sequence as set forth in SEQ ID NO: 100; c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A5A* gene, to effect increased production of dicarboxylic acid.

A method for increasing the production of a *CYP52A5A* protein having an amino acid sequence as set forth in SEQ ID NO: 100 is provided which includes a) transforming a host cell having a naturally occurring amount of *CYP52A5A* protein with an increased copy number of a *CYP52A5A* gene that encodes the *CYP52A5A* protein having the amino acid sequence as set forth in SEQ ID NO: 100; and b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A5A* gene.

A method for increasing production of a dicarboxylic acid is provided which includes a) providing a host cell having a naturally occurring number of *CYP52A5B* genes; b) increasing, in the host cell, the number of *CYP52A5B* genes which encode a *CYP52A5B* protein having the amino acid sequence as set forth in SEQ ID NO: 101; c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A5B* gene, to effect increased production of dicarboxylic acid.

A method for increasing the production of a *CYP52A5B* protein having an amino acid sequence as set forth in SEQ ID NO: 101 is provided which includes a) transforming a host cell having a naturally occurring amount of *CYP52A5B* protein with an increased copy number of a *CYP52A5B* gene that encodes the *CYP52A5B* protein having the amino acid sequence as set forth in SEQ ID NO: 101; and b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A5B* gene.

A method for increasing production of a dicarboxylic acid is provided which includes a) providing a host cell having a naturally occurring number of *CYP52A8A* genes; b) increasing, in the host cell, the number of *CYP52A8A* genes which encode a *CYP52A8A* protein having the amino acid sequence as set forth in SEQ ID NO: 102; c) culturing the host cell in

media containing an organic substrate which upregulates the *CYP52A8A* gene, to effect increased production of dicarboxylic acid.

A method for increasing the production of a *CYP52A8A* protein having an amino acid sequence as set forth in SEQ ID NO: 102 is provided which includes a) transforming a host cell having a naturally occurring amount of *CYP52A8A* protein with an increased copy number of a *CYP52A8A* gene that encodes the *CYP52A8A* protein having the amino acid sequence as set forth in SEQ ID NO: 102; and b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A8A* gene.

A method for increasing production of a dicarboxylic acid is provided which includes a) providing a host cell having a naturally occurring number of *CYP52A8B* genes; b) increasing, in the host cell, the number of *CYP52A8B* genes which encode a *CYP52A8B* protein having the amino acid sequence as set forth in SEQ ID NO: 103; c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A8B* gene, to effect increased production of dicarboxylic acid.

A method for increasing the production of a *CYP52A8B* protein having an amino acid sequence as set forth in SEQ ID NO: 103 is provided which includes a) transforming a host cell having a naturally occurring amount of *CYP52A8B* protein with an increased copy number of a *CYP52A8B* gene that encodes the *CYP52A8B* protein having the amino acid sequence as set forth in SEQ ID NO: 103; and b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A8B* gene.

A method for increasing production of a dicarboxylic acid is provided which includes a) providing a host cell having a naturally occurring number of *CYP52D4A* genes; b) increasing, in the host cell, the number of *CYP52D4A* genes which encode a *CYP52D4A* protein having the amino acid sequence as set forth in SEQ ID NO: 104; c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52D4A* gene, to effect increased production of dicarboxylic acid.

A method for increasing the production of a *CYP52D4A* protein having an amino acid sequence as set forth in SEQ ID NO: 104 is provided which includes a) transforming a host cell having a naturally occurring amount of *CYP52D4A* protein with an increased copy number

of a *CYP52D4A* gene that encodes the *CYP52D4A* protein having the amino acid sequence as set forth in SEQ ID NO: 104; and b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52D4A* gene.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic representation of cloning vector pTriplEx from Clontech™ Laboratories, Inc. Selected restriction sites within the multiple cloning site are shown.

Figure 2A is a map of the ZAP Express™ vector.

Figure 2B is a schematic representation of cloning phagemid vector pBK-CMV.

Figure 3 is a double stranded DNA sequence of a portion of the 5 prime coding region of the *CYP52A5A* gene (SEQ ID NO: 36).

Figure 4 is a diagrammatic representation of highly conserved regions of *CYP* and *CPR* gene protein sequences. Helix I represents the putative substrate binding site and HR2 represents the heme binding region. The FMN, FAD and NADPH binding regions are indicated below the *CPR* gene.

Figure 5 is a diagrammatic representation of the plasmid pHKM1 containing the truncated *CPRA* gene present in the pTriplEx vector. A detailed restriction map of only the sequenced region is shown at the top. The bar indicates the open reading frame. The direction of transcription is indicated by an arrow under the open reading frame.

Figure 6 is a diagrammatic representation of the plasmid pHKM4 containing the truncated *CPRA* gene present in the pTriplEx vector. A detailed restriction map of only the sequenced region is shown at the top. The bar indicates the open reading frame. The direction of transcription is indicated by an arrow under the open reading frame.

Figure 7 is a diagrammatic representation of the plasmid pHKM9 containing the *CPRB* gene (SEQ ID NO: 82) present in the pBK-CMV vector. A detailed restriction map of only the sequenced region is shown at the top. The bar indicates the open reading frame. The direction of transcription is indicated by an arrow under the open reading frame.

Figure 8 is a diagrammatic representation of the plasmid pHKM11 containing the *CYP52A1A* gene (SEQ ID NO: 85) present in the pBK-CMV vector. A detailed restriction map

of only the sequenced region is shown at the top. The bar indicates the open reading frame. The direction of transcription is indicated by an arrow under the open reading frame.

Figure 9 is a diagrammatic representation of the plasmid pHKM12 containing the *CYP52A8A* gene (SEQ ID NO: 92) present in the pBK-CMV vector. A detailed restriction map of only the sequenced region is shown at the top. The bar indicates the open reading frame. The direction of transcription is indicated by an arrow under the open reading frame.

Figure 10 is a diagrammatic representation of the plasmid pHKM13 containing the *CYP52D4A* gene (SEQ ID NO: 94) present in the pBK-CMV vector. A detailed restriction map of only the sequenced region is shown at the top. The bar indicates the open reading frame. The direction of transcription is indicated by an arrow under the open reading frame.

Figure 11 is a diagrammatic representation of the plasmid pHKM14 containing the *CYP52A2B* gene (SEQ ID NO: 87) present in the pBK-CMV vector. A detailed restriction map of only the sequenced region is shown at the top. The bar indicates the open reading frame. The direction of transcription is indicated by an arrow under the open reading frame.

Figure 12 is a diagrammatic representation of the plasmid pHKM15 containing the *CYP52A8B* gene (SEQ ID NO: 93) present in the pBK-CMV vector. A detailed restriction map of only the sequenced region is shown at the top. The bar indicates the open reading frame. The direction of transcription is indicated by an arrow under the open reading frame.

Figures 13A-13D show the complete DNA sequences including regulatory and coding regions for the *CPRA* gene (SEQ ID NO: 81) and *CPRB* gene (SEQ ID NO: 82) from *C. tropicalis* ATCC 20336. Figures 13A-13D show regulatory and coding region alignment of these sequences. Asterisks indicate conserved nucleotides. Bold indicates protein coding nucleotides; the start and stop codons are underlined.

Figure 14 shows the amino acid sequence of the *CPRA* (SEQ ID NO: 83) and *CPRB* (SEQ ID NO: 84) proteins from *C. tropicalis* ATCC 20336 and alignment of these amino acid sequences. Asterisks indicate residues which are not conserved.

Figures 15A-15M show the complete DNA sequences including regulatory and coding regions for the following genes from *C. tropicalis* ATCC 20366: *CYP52A1A* (SEQ ID NO: 85), *CYP52A2A* (SEQ ID NO: 86), *CYP52A2B* (SEQ ID NO: 87), *CYP52A3A* (SEQ ID NO: 88), *CYP52A3B* (SEQ ID NO: 89), *CYP52A5A* (SEQ ID NO. 90), *CYP52A5B* (SEQ ID NO: 91), *CYP52A8A* (SEQ ID NO: 92), *CYP52A8B* (SEQ ID NO: 93), and *CYP52D4*A (SEQ ID NO: 94).

Figures 15A-15M show regulatory and coding region alignment of these sequences. Asterisks indicate conserved nucleotides. Bold indicates protein coding nucleotides; the start and stop codons are underlined.

Figures 16A-16C show the amino acid sequences encoding the *CYP52A1A* (SEQ ID NO: 95), *CYP52A2A* (SEQ ID NO: 96), *CYP52A2B* (SEQ ID NO: 97), *CYP52A3A* (SEQ ID NO: 98), *CYP52A3B* (SEQ ID NO: 99), *CYP52A5A* (SEQ ID NO: 100), *CYP52A5B* (SEQ ID NO: 101), *CYP52A8A* (SEQ ID NO: 102), *CYP52A8B* (SEQ ID NO: 103) and *CYP52D4A* (SEQ ID NO. 104) proteins from *C. tropicalis* ATCC 20336. Asterisks indicate identical residues and dots indicate conserved residues.

Figure 17 is a diagrammatic representation of the pTAg PCR product cloning vector (commercially available from R&D Systems, Minneapolis, MN).

Figure 18 is a plot of the log ratio (U/C) of unknown target DNA product to competitor DNA product versus the concentration of competitor mRNA. The plot is used to calculate the target messenger RNA concentration in a quantitative competitive reverse transcription polymerase chain reaction (QC-RT-PCR).

Figure 19 is a graph showing the relative induction of *C. tropicalis* ATCC 20962 *CYP52A5A* (SEQ ID NO: 90) by the addition of the fatty acid substrate Emersol® 267 to the growth medium.

Figure 20 is a graph showing the induction of *C. tropicalis* ATCC 20962 *CYP52* and *CPR* genes by Emersol® 267. P450 genes *CYP52A3A* (SEQ ID NO: 88), *CYP52A3B* (SEQ ID NO: 89), and *CYP52D4A* (SEQ ID NO: 94) are expressed at levels below the detection level of the QC-RT-PCR assay.

Figure 21 is a scheme to integrate selected genes into the genome of *Candida tropicalis* strains and recovery of *URA3A* selectable marker.

Figure 22 is a schematic representation of the transformation of *C. tropicalis* H5343 ura3⁻ with *CYP* and/or *CPR* genes. Only one *URA3* locus needs to be functional. There are a total of 6 possible *ura*3 targets (5*ura*3A loci-2 pox4 disruptions, 2 pox 5 disruptions, 1 *ura*3A locus; and 1 *ura*3B locus).

Figure 23 is the complete DNA sequence (SEQ ID NO: 105) encoding *URA3A* from *C. tropicalis* ATCC 20336 and the amino acid sequence of the encoded protein (SEQ ID NO: 106).

Figure 24 is a schematic representation of the plasmid pURAin, the base vector for integrating selected genes into the genome of *C. tropicalis*. The detailed construction of pURAin is described in the text.

Figure 25 is a schematic representation of the plasmid pNEB193 cloning vector (commercially available from New England Biolabs, Beverly, MA).

Figure 26 is a diagrammatic representation of the plasmid pPA15 containing the truncated *CYP52A2A* gene present in the pTriplEx vector. A detailed restriction map of only the sequenced region is shown at the top. The bar indicates the open reading frame. The direction of transcription is indicated by an arrow under the open reading frame.

Figure 27 is a schematic representation of pURA2in, the base vector is constructed in pNEB193 which contains the 8 bp recognition sequences for *Asc I, Pac I* and *Pme I*. *URA3A* (SEQ ID NO: 105) and *CYP52A2A* (SEQ ID NO: 86) do not contain these 8 bp recognition sites. *URA3A* is inverted so that the transforming fragment will attempt to recircularize prior to integration. An *Asc I/Pme I* fragment was used to transform H5343 ura⁻.

Figure 28 shows a scheme to detect integration of *CYP52A2A* gene (SEQ ID NO: 86) into the genome of H5343 ura⁻. In all cases, hybridization band intensity could reflect the number of integrations.

Figure 29 is a diagrammatic representation of the plasmid pPA57 containing the truncated *CYP52A3A* gene present in the pTriplEx vector. A detailed restriction map of only the sequenced region is shown at the top. The bar indicates the open reading frame. The direction of transcription is indicated by an arrow under the open reading frame.

Figure 30 is a diagrammatic representation of the plasmid pPA62 containing the truncated *CYP52A3B* gene present in the pTriplEx vector. A detailed restriction map of only the sequenced region is shown at the top. The bar indicates the open reading frame. The direction of transcription is indicated by an arrow under the open reading frame.

Figure 31 is a diagrammatic representation of the plasmid pPAL3 containing the truncated *CYP52A5A* gene present in the pTriplEx vector. A detailed restriction map of only the sequenced region is shown at the top. The bar indicates the open reading frame. The direction of transcription is indicated by an arrow under the open reading frame.

Figure 32 is a diagrammatic representation of the plasmid pPA5 containing the truncated *CYP52A5A* gene present in the pTriplEx vector. A detailed restriction map of only the

sequenced region is shown at the top. The bar indicates the open reading frame. The direction of transcription is indicated by an arrow under the open reading frame.

Figure 33 is a diagrammatic representation of the plasmid pPA18 containing the truncated *CYP52D4A* gene present in the pTriplEx vector. A detailed restriction map of only the sequenced region is shown at the top. The bar indicates the open reading frame. The direction of transcription is indicated by an arrow under the open reading frame.

Figure 34 is a graph showing the expression of *CYP52A1* (SEQ ID NO: 85), *CYP52A2* (SEQ ID NO: 86) and *CYP52A5* genes (SEQ ID NOS: 90 and 91) from *C. tropicalis* 20962 in a fermentor run upon the addition of amounts of the substrate oleic acid or tridecane in a spiking experiment.

Figure 35 depicts a scheme used for the extraction and analysis of diacids and monoacids from fermentation broths.

Figure 36 is a graph showing the induction of expression of *CYP52A1A*, *CYP52A2A* and *CYP52A5A* in a fermentor run upon addition of the substrate octadecane. No induction of *CYP52A3A* or *CYP52A3B* was observed under these conditions.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

Diacid productivity is improved according to the present invention by selectively increasing enzymes which are known to be important to the oxidation of organic substrates such as fatty acids composing the desired feed. According to the present invention, ten *CYP* genes and two *CPR* genes of *C. tropicalis* have been identified and characterized that relate to participation in the ω-hydroxylase complex catalyzing the first step in the ω-oxidation pathway. In addition, a novel quantitative competitive reverse transcription polymerase chain reaction (QC-RT-PCR) assay is used to measure gene expression in the fermentor under conditions of induction by one or more organic substrates as defined herein. Based upon QC-RT-PCR results, three *CYP* genes, *CYP52A1*, *CYP52A2* and *CYP52A5*, have been identified as being of greater importance for the ω-oxidation of long chain fatty acids. Amplification of the *CPR* gene copy number improves productivity. The QC-RT-PCR assay indicates that both *CYP* and *CPR* genes appear to be under tight regulatory control.

In accordance with the present invention, a method for discriminating members of a gene family by quantifying the amount of target mRNA in a sample is provided which

includes a) providing an organism containing a target gene; b) culturing the organism with an organic substrate which causes upregulation in the activity of the target gene; c) obtaining a sample of total RNA from the organism at a first point in time; d) combining at least a portion of the sample of the total RNA with a known amount of competitor RNA to form an RNA mixture, wherein the competitor RNA is substantially similar to the target mRNA but has a lesser number of nucleotides compared to the target mRNA; e) adding reverse transcriptase to the RNA mixture in a quantity sufficient to form corresponding target DNA and competitor DNA; (f) conducting a polymerase chain reaction in the presence of at least one primer specific for at least one substantially non-homologous region of the target DNA within the gene family, the primer also specific for the competitor DNA; g) repeating steps (c-f) using increasing amounts of the competitor RNA while maintaining a substantially constant amount of target RNA; h) determining the point at which the amount of target DNA is substantially equal to the amount of competitor DNA; i) quantifying the results by comparing the ratio of the concentration of unknown target to the known concentration of competitor; and j) obtaining a sample of total RNA from the organism at another point in time and repeating steps (d-i).

In addition, modification of existing promoters and/or the isolation of alternative promoters provides increased expression of *CYP* and *CPR* genes. Strong promoters are obtained from at least four sources: random or specific modifications of the *CYP52A2* promoter, *CYP52A5* promoter, *CYP52A1* promoter, the selection of a strong promoter from available *Candida* β-oxidation genes such as *POX4* and *POX5,* or screening to select another suitable *Candida* promoter.

Promoter strength can be directly measured using QT-RT-PCR to measure *CYP* and *CPR* gene expression in *Candida* cells isolated from fermentors. Enzymatic assays and antibodies specific for *CYP* and *CPR* proteins are used to verify that increased promoter strength is reflected by increased synthesis of the corresponding enzymes. Once a suitable promoter is identified, it is fused to the selected *CYP* and *CPR* genes and introduced into *Candida* for construction of a new improved production strain. It is contemplated that the coding region of the *CYP* and *CPR* genes can be fused to suitable promoters or other regulatory sequences which are well known to those skilled in the art.

In accordance with the present invention, studies on *C. tropicalis* ATCC 20336 have identified six unique *CYP* genes and four potential alleles. QC-RT-PCR analyses of cells

isolated during the course of the fermentation bioconversions indicate that at least three of the *CYP* genes are induced by fatty acids and at least two of the *CYP* genes are induced by alkanes. See Figure 34. Two of the *CYP* genes are highly induced indicating participation in the ω-hydroxylase complex which catalyzes the rate limiting step in the oxidation of fatty acids to the corresponding diacids.

The biochemical characterizations of each P450 enzyme herein is used to tailor the *C. tropicalis* host for optimal diacid productivity and is used to select P450 enzymes to be amplified based upon the fatty acid content of the feedstream. *CYP* gene(s) encoding P450 enzymes that have a low specific activity for the fatty acid or alkane substrate of choice are targeted for inactivation, thereby reducing the physiological load on the cell.

Since it has been demonstrated that *CPR* can be limiting in yeast systems, the removal of non-essential P450s from the system can free electrons that are being used by non-essential P450s and make them available to the P450s important for diacid productivity. Moreover, the removal of non-essential P450s can make available other necessary but potentially limiting components of the P450 system (i.e., available membrane space, heme and/or NADPH).

Diacid productivity is thus improved by selective integration, amplification, and over expression of *CYP* and *CPR* genes in the C. *tropicalis* production host.

It should be understood that host cells into which one or more copies of desired *CYP* and/or *CPR* genes have been introduced can be made to include such genes by any technique known to those skilled in the art. For example, suitable host cells include procaryotes such as *Bacillus sp.*, *Pseudomous sp.*, *Actinomycetes sp.*, *Eschericia sp.*, *Mycobacterium sp.*, and eukaryotes such as yeast, algae, insect cells, plant cells and and filamentous fungi. Suitable host cells are preferably yeast cells such as *Yarrowia*, *Bebaromyces*, *Saccharomyces*, *Schizosaccharomyces*, and *Pichia* and more preferably those of the *Candida* genus. Preferred species of *Candida* are *tropicalis*, *maltosa*, *apicola*, *paratropicalis*, *albicans*, *cloacae*, *guillermondii*, *intermedia*, *lipolytica*, *parapsilosis* and *zeylenoides*. Certain preferred stains of *Candida tropicalis* are listed in U.S. Patent No. 5,254,466, incorporated herein by reference.

Vectors such as plasmids, phagemids, phages or cosmids can be used to transform or transfect suitable host cells. Host cells may also be transformed by introducing into a cell a linear DNA vector(s) containing the desired gene sequence. Such linear DNA may be advantageous when it is desirable to avoid introduction of non-native (foreign) DNA into the

cell. For example, DNA consisting of a desired target gene(s) flanked by DNA sequences which are native to the cell can be introduced into the cell by electroporation, lithium acetate transformation, spheroplasting and the like. Flanking DNA sequences can include selectable markers and/or other tools for genetic engineering.

A suitable organic substrate herein can be any organic compound that is biooxidizable to a mono- or polycarboxylic acid. Such a compound can be any saturated or unsaturated aliphatic compound or any carbocyclic or heterocyclic aromatic compound having at least one terminal methyl group, a terminal carboxyl group and/or a terminal functional group which is oxidizable to a carboxyl group by biooxidation. A terminal functional group which is a derivative of a carboxyl group may be present in the substrate molecule and may be converted to a carboxyl group by a reaction other than biooxidation. For example, if the terminal group is an ester that neither the wild-type *C. tropicalis* nor the genetic modifications described herein will allow hydrolysis of the ester functionality to a carboxyl group, then a lipase can be added during the fermentation step to liberate free fatty acids. Suitable organic substrates include, but are not limited to, saturated fatty acids, unsaturated fatty acids, alkanes, alkenes, alkynes and combinations thereof.

Alkanes are a type of saturated organic substrate which are useful herein. The alkanes can be linear or cyclic, branched or straight chain, substituted or unsubstituted. Particularly preferred alkanes are those having from about 4 to about 25 carbon atoms, examples of which include but are not limited to butane, hexane, octane, nonane, dodecane, tridecane, tetradecane, octadecane and the like.

Examples of unsaturated organic substrates which can be used herein include but are not limited to internal olefins such as 2-pentene, 2-hexene, 3-hexene, 9-octadecene and the like; unsaturated carboxylic acids such as 2-hexenoic acid and esters thereof, oleic acid and esters thereof including triglyceryl esters having a relatively high oleic acid content, erucic acid and esters thereof including triglyceryl esters having a relatively high erucic acid content, ricinoleic acid and esters thereof including triglyceryl esters having a relatively high ricinoleic acid content, linoleic acid and esters thereof including triglyceryl esters having a relatively high linoleic acid content; unsaturated alcohols such as 3-hexen-1-ol, 9-octadecen-1-ol and the like; unsaturated aldehydes such as 3-hexen-1-al, 9-octadecen-1-al and the like. In addition to the above, an organic substrate which can be used herein include alicyclic compounds having at least one

internal carbon-carbon double bond and at least one terminal methyl group, a terminal carboxyl group and/or a terminal functional group which is oxidizable to a carboxyl group by biooxidation. Examples of such compounds include but are not limited to 3,6-dimethyl, 1,4-cyclohexadiene; 3-methylcyclohexene; 3-methyl-1, 4-cyclohexadiene and the like.

Examples of the aromatic compounds that can be used herein include but are not limited to arenes such as o-, m-, p-xylene; o-, m-, p-methyl benzoic acid; dimethyl pyridine, and the like. The organic substrate can also contain other functional groups that are biooxidizable to carboxyl groups such as an aldehyde or alcohol group. The organic substrate can also contain other functional groups that are not biooxidizable to carboxyl groups and do not interfere with the biooxidation such as halogens, ethers, and the like.

Examples of saturated fatty acids which may be applied to cells incorporating the present *CYP* and *CPR* genes include caproic, enanthic, caprylic, pelargonic, capric, undecylic, lauric, myristic, pentadecanoic, palmitic, margaric, stearic, arachidic, behenic acids and combinations thereof. Examples of unsaturated fatty acids which may be applied to cells incorporating the present *CYP* and *CPR* genes include palmitoleic, oleic, erucic, linoleic, linolenic acids and combinations thereof. Alkanes and fractions of alkanes may be applied which include chain links from C12 to C24 in any combination. An example of a preferred fatty acid mixtures are Emersol® 267 and Tallow, both commercially available from Henkel Chemicals Group, Cincinnati, OH. The typical fatty acid composition of Emersol® 267 and Tallow is as follows:

	TALLOW	E267
C14:0	3.5%	2.4%
C14:1	1.0%	0.7%
C15:0	0.5%	-------
C16:0	25.5%	4.6%
C16:1	4.0%	5.7%
C17:0	2.5%	-------
C17:1	-------	5.7%
C18:0	19.5%	1.0%
C18:1	41.0%	69.9%
C18:2	2.5%	8.8%

C18:3	-------	0.3%
C20:0	0.5%	-------
C20:1	-------	0.9%

The following examples are meant to illustrate but not to limit the invention. All relevant microbial strains and plasmids are described in Table 1 and Table 2, respectively.

Table 1. List of *Escherichia coli* and *Candida tropicalis* strains

E. Coli STRAIN	GENOTYPE	SOURCE
XL1Blue-MRF'	*endA1, gyrA96, hsdR17, lac*$^-$, *recA1, relA1, supE44, thi-1,* [F' *lacI*^{q}*Z M15, proAB,* Tn*10*]	Stratagene, La Jolla, CA
BM25.8	*SupE44, thi (lac-proAB)* [F' *traD36, proAB*$^+$, *lacI*^{q}*Z M15*] λ*imm434 (kan*^{R}*)P1 (cam*^{R}*) hsdR (r*$_{k12}^-$ *m*$_{k12}^-$*)*	Clontech, Palo Alto, CA
XLOLR	*(mcrA)183 (mcrCB-hsdSMR-mrr)173 endA1 thi-1 recA1 gyrA96 relA1 lac* [F'*proAB lacI*^{q}*Z M15* Tn*10* (Tet^r) Su$^-$ (nonsuppressing λ^r(lambda resistant)	Stratagene, La Jolla, CA

C. tropicalis STRAIN	GENOTYPE	SOURCE
ATCC20336	Wild-type	American Type Culture Collection, Rockville, MD
ATCC750	Wild-type	American Type Culture Collection, Rockville, MD
ATCC 20962	*ura3A/ura3B, pox4A::ura3A/pox4B::ura3A, pox5::ura3A/pox5::URA3A*	Henkel
H5343 ura-	*ura3A/ura3B, pox4A::ura3A/pox4B::ura3A, pox5::ura3A/pox5::URA3A, ura3-*	Henkel
HDC1	*ura3A/ura3B, pox4A::ura3A/pox4B::ura3A, pox5::ura3A/pox5::URA3A, ura3::URA3A-CYP52A2A*	Henkel
HDC5	*ura3A/ura3B, pox4A::ura3A/pox4B::ura3A, pox5::ura3A/pox5::URA3A, ura3::URA3A-CYP52A3A*	Henkel
HDC10	*ura3A/ura3B, pox4A::ura3A/pox4B::ura3A, pox5::ura3A/pox5::URA3A, ura3::URA3A-CPRB*	Henkel

HDC15	*ura3A/ura3B, pox4A::ura3A/pox4B::ura3A, pox5::ura3A/pox5::URA3A, ura3::URA3A-CYP52A5A*	Henkel
HDC20	*ura3A/ura3B, pox4A::ura3A/pox4B::ura3A, pox5::ura3A/pox5::URA3A, ura3::URA3A-CYP52A2A + CPR B* (*CYP* and *CPR* have opposite 5' to 3' orientation with respect to each other)	Henkel
HDC23	*ura3A/ura3B, pox4A::ura3A/pox4B::ura3A, pox5::ura3A/pox5::URA3A, ura3::URA3A-CYP52A2A + CPR B* (*CYP* and *CPR* have same 5' to 3' orientation with respect to each other)	Henkel

Table 2. List of plasmids isolated from genomic libraries and constructed for use in gene integrations.

Plasmid	Base vector	Insert	Insert Size	Plasmid size	Description
pURAin	pNEB193	*URA3A*	1706 bp	4399 bp	pNEB193 with the *URA3A* gene inserted in the *AscI - PmeI* site, generating a *PacI* site
pURA 2in	pURAin	*CYP52A2A*	2230 bp	6629 bp	pURAin containing a PCR *CYP52A2A* allele containing *PacI* restriction sites
pURA REDB in	pURAin	*CPRB*	3266 bp	7665 bp	pURAin containing a PCR *CPRB* allele containing *PacI* restriction sites
pHKM1	pTriplEx	Truncated *CPRA* gene	Approx. 3.8 kb	Approx. 7.4 kb	A truncated *CPRA* gene obtained by first screening library containing the 5' untranslated region and 1.2 kb open reading frame
pHKM4	PTriplEx	Truncated *CPRA* gene	Approx. 5 kb	Approx. 8.6 kb	A truncated *CPRA* gene obtained by screening second library containing the 3' untranslated region end sequence
pHKM9	pBC-CMV	*CPRB* gene	Approx. 5.3 kb	Approx. 9.8 kb	*CPRB* allele isolated from the third library
pHKM11	pBC-CMV	*CYP52A1A*	Approx. 5 kb	Approx. 9.5 kb	*CYP52A1A* isolated from the third library
pHKM12	pBC-CMV	*CYP52A8A*	Approx. 7.5 kb	Approx. 12 kb	*CYP52A8A* isolated from the third library
pHKM13	pBC-CMV	*CYP52D4A*	Approx. 7.3 kb	Approx. 11.8 kb	*CYP52D4A* isolated from the third library

pHKM14	pBC-CMV	*CYP52A2B*	Approx. 6 kb	Approx. 10.5 kb	*CYP52A2B* isolated from the third library
pHKM15	pBC-CMV	*CYP52A8B*	Approx. 6.6 kb	Approx. 11.1 kb	*CYP52A8B* isolated from the third library
pPAL3	pTriplEx	*CYP52A5A*	4.4 kb	Approx. 8.1 kb	*CYP52A5A* isolated from the 1st library
pPA5	pTriplEx	*CYP52A5B*	4.1 kb	Approx. 7.8 kb	*CYP52A5B* isolated from the 2nd library
pPA15	pTriplEx	*CYP52A2A*	6.0 kb	Approx. 9.7 kb	*CYP52A2A* isolated from the 2nd library
pPA57	pTriplEx	*CYP52A3A*	5.5 kb	Approx. 9.2 kb	*CYP52A3A* isolated from the 2nd library
pPA62	pTriplEx	*CYP52A3B*	6.0 kb	Approx. 9.7 kb	*CYP52A3B* isolated from the 2nd library

EXAMPLE 1

Purification of Genomic DNA from *Candida tropicalis* ATCC 20336

A. Construction of Genomic Libraries

50 ml of YEPD broth (see Chart) was inoculated with a single colony of *C. tropicalis* 20336 from YEPD agar plate and grown overnight at 30°C. 5 ml of the overnight culture was inoculated into 100 ml of fresh YEPD broth and incubated at 30°C for 4 to 5 hr with shaking. Cells were harvested by centrifugation, washed twice with sterile distilled water and resuspended in 4 ml of spheroplasting buffer (1 M Sorbitol, 50 mM EDTA, 14 mM mercaptoethanol) and incubated for 30 min at 37°C with gentle shaking. 0.5 ml of 2 mg/ml zymolyase (ICN Pharmaceuticals, Inc., Irvine, CA) was added and incubated at 37°C with gentle shaking for 30 to 60 min. Spheroplast formation was monitored by SDS lysis. Spheroplasts were harvested by brief centrifugation (4,000 rpm, 3 min) and were washed once with the spheroplast buffer without mercaptoethanol. Harvested spheroplasts were then suspended in 4 ml of lysis buffer (0.2 M Tris/pH 8.0, 50 mM EDTA, 1% SDS) containing 100 µg/ml RNase (Qiagen Inc., Chatsworth, CA) and incubated at 37°C for 30 to 60 min.

Proteins were denatured and extracted twice with an equal volume of chloroform/isoamyl alcohol (24:1) by gently mixing the two phases by hand inversions. The two phases were separated by centrifugation at 10,000 rpm for 10 min and the aqueous phase containing the high-molecular weight DNA was recovered. To the aqueous layer NaCl was added to a final concentration of 0.2 M and the DNA was precipitated by adding 2 vol of ethanol. Precipitated DNA was spooled with a clean glass rod and resuspended in TE buffer (10 mM

Tris/pH 8.0, 1 mM EDTA) and allowed to dissolve overnight at 4°C. To the dissolved DNA, RNase free of any DNase activity (Qiagen Inc., Chatsworth, CA) was added to a final concentration of 50 µg/ml and incubated at 37°C for 30 min. Then protease (Qiagen Inc., Chatsworth, CA) was added to a final concentration of 100 µg/ml and incubated at 55 to 60°C for 30 min. The solution was extracted once with an equal volume of phenol/chloroform/isoamyl alcohol (25:24:1) and once with equal volume of chloroform/isoamyl alcohol (24:1). To the aqueous phase 0.1 vol of 3 M sodium acetate and 2 volumes of ice cold ethanol (200 proof) were added and the high molecular weight DNA was spooled with a glass rod and dissolved in 1 to 2 ml of TE buffer.

B. Genomic DNA Preparation for PCR Amplification of *CYP* and *CPR* Genes

Five 5 ml of YPD medium was inoculated with a single colony and grown at 30°C overnight. The culture was centrifuged for 5 min at 1200 x g. The supernatant was removed by aspiration and 0.5 ml of a sorbitol solution (0.9 M sorbitol, 0.1 M Tris-Cl pH 8.0, 0.1 M EDTA) was added to the pellet. The pellet was resuspended by vortexing and 1 µl of 2-mercaptoethanol and 50 µl of a 10 µg/ml zymolyase solution were added to the mixture. The tube was incubated at 37°C for 1 hr on a rotary shaker (200 rpm). The tube was then centrifuged for 5 min at 1200 x g and the supernatant was removed by aspiration. The protoplast pellet was resuspended in 0.5 ml 1x TE (10 mM Tris-Cl pH 8.0, 1 mM EDTA) and transferred to a 1.5 ml microcentrifuge tube. The protoplasts were lysed by the addition of 50 µl 10% SDS followed by incubation at 65°C for 20 min. Next, 200 µl of 5M potassium acetate was added and after mixing, the tube was incubated on ice for at least 30 min. Cellular debris was removed by centrifugation at 13,000 x g for 5 min. The supernatant was carefully removed and transferred to a new microfuge tube. The DNA was precipitated by the addition of 1 ml 100% (200 proof) ethanol followed by centrifugation for 5 min at 13,000 x g. The DNA pellet was washed with 1 ml 70 % ethanol followed by centrifugation for 5 min at 13,000 x g. After partially drying the DNA under a vacuum, it was resuspended in 200 µl of 1x TE. The DNA concentration was determined by ratio of the absorbance at 260 nm / 280 nm ($A_{260/280}$).

EXAMPLE 2

Construction of *Candida tropicalis* 20336 Genomic Libraries

Three genomic libraries of *C. tropicalis* were constructed, two at Clontech Laboratories, Inc., (Palo Alto, CA) and one at Henkel Corporation (Cincinnati, OH).

A. Clontech Libraries

The first Clontech library was made as follows: Genomic DNA was prepared from *C. tropicalis* 20336 as described above, partially digested with *Eco*RI and size fractionated by gel electrophoresis to eliminate fragments smaller than 0.6 kb. Following size fractionation, several ligations of the *Eco*RI genomic DNA fragments and lambda (λ) TriplEx™ vector (Figure 1) arms with *Eco*RI sticky ends were packaged into λ phage heads under conditions designed to obtain one million independent clones. The second genomic library was constructed as follows: Genomic DNA was digested partially with *Sau3A1* and size fractionated by gel electrophoresis. The DNA fragments were blunt ended using standard protocols as described, e.g., in Sambrook et al, *Molecular Cloning: A Laboratory Manual*, 2ed. Cold Spring Harbor Press, USA (1989), incorporated herein by reference. The strategy was to fill in the *Sau3A1* overhangs with Klenow polymerase (Life Technologies, Grand Island, NY) followed by digestion with S1 nuclease (Life Technologies, Grand Island, NY). After S1 nuclease digestion the fragments were end filled one more time with Klenow polymerase to obtain the final blunt-ended DNA fragments. *Eco*RI linkers were ligated to these blunt-ended DNA fragments followed by ligation into the λTriplEx vector. The resultant library contained approximately 2 X 10^6 independent clones with an average insert size of 4.5 kb.

B. Henkel Library

The third genomic library was constructed at Henkel Corporation using λZAP Express™ vector (Stratagene, La Jolla, CA) (Figure 2). Genomic DNA was partially digested with *Sau3A1* and fragments in the range of 6 to 12 kb were purified from an agarose gel after electrophoresis of the digested DNA. These DNA fragments were then ligated to *Bam*HI digested λZAP Express™ vector arms according to manufacturers protocols. Three ligations were set up to obtain approximately 9.8 X 10^5 independent clones. All three libraries were pooled and amplified according to manufacturer instructions to obtain high-titre (>10^9 plaque

forming units/ml) stock for long-term storage. The titre of packaged phage library was ascertained after infection of *E. coli* XL1Blue-MRF' cells. *E. coli* XL1Blue-MRF' were grown overnight in either in LB medium or NZCYM (Chart) containing 10 mM $MgSO_4$ and 0.2% maltose at 37°C or 30°C, respectively with shaking. Cells were then centrifuged and resuspended in 0.5 to 1 volume of 10 mM $MgSO_4$. 200 µl of this *E. coli* culture was mixed with several dilutions of packaged phage library and incubated at 37°C for 15 min. To this mixture 2.5 ml of LB top agarose or NZCYM top agarose (maintained at 60°C) (see Chart) was added and plated on LB agar or NCZYM agar (see Chart) present in 82 mm petri dishes. Phage were allowed to propagate overnight at 37°C to obtain discrete plaques and the phage titre was determined.

EXAMPLE 3

Screening of Genomic Libraries

Both λTriplEx™ and λZAP Express™ vectors are phagemid vectors that can be propagated either as phage or plasmid DNA (after conversion of phage to plasmid). Therefore, the genomic libraries constructed in these vectors can be screened either by plaque hybridization (screening of lambda form of library) or by colony hybridization (screening plasmid form of library after phage to plasmid conversion). Both vectors are capable of expressing the cloned genes and the main difference is the mechanism of excision of plasmid from the phage DNA. The cloning site in λTriplEx™ is located within a plasmid which is present in the phage and is flanked by *loxP* site (Figure 1). When λTriplEx™ is introduced into *E. coli* strain BM25.8 (supplied by Clontech), the *Cre* recombinase present in BM25.8 promotes the excision and circularization of plasmid pTriplEx from the phage λTriplEx™ at the *loxP* sites. The mechanism of excision of plasmid pBK-CMV from phage λZAP Express™ is different. It requires the assistance of a helper phage such as ExAssist™ (Stratagene) and an *E. coli* strain such as XLOR (Stratagene). Both pTriplEx and pBK-CMVcan replicate autonomously in *E. coli*.

A. Screening Genomic Libraries (Plasmid Form)

1) Colony Lifts

A single colony of *E. coli* BM25.8 was inoculated into 5 ml of LB containing 50 µg/ml kanamycin, 10 mM $MgSO_4$ and 0.1% maltose and grown overnight at 31 °C, 250 rpm. To 200 µl of this overnight culture (~ 4 X 10^8 cells) 1 µl of phage library (2 - 5 X 10^6 plaque forming units) and 150 µl LB broth were added and incubated at 31 °C for 30 min after which 400 µl of LB broth was added and incubated at 31 °C , 225 rpm for 1 h. This bacterial culture was diluted and plated on LB agar containing 50 µg/ml ampicillin (Sigma Chemical Company, St. Louis, MO) and kanamycin (Sigma Chemical Company) to obtain 500 to 600 colonies/plate. The plates were incubated at 37°C for 6 to 7 hrs until the colonies became visible. The plates were then stored at 4 °C for 1.5 h before placing a Colony/Plaque Screen™ Hybridization Transfer Membrane disc (DuPont NEN Research Products, Boston, MA) on the plate in contact with bacterial colonies. The transfer of colonies to the membrane was allowed to proceed for 3 to 5 min. The membrane was then lifted and placed on a fresh LB agar (see Chart) plate containing 200 µg/ml of chloramphenicol with the side exposed to the bacterial colonies facing up. The plates containing the membranes were then incubated at 37°C overnight in order to allow full development of the bacterial colonies. The LB agar plates from which colonies were initially lifted were incubated at 37°C overnight and stored at 4 °C for future use. The following morning the membranes containing bacterial colonies were lifted and placed on two sheets of Whatman 3M (Whatman, Hillsboro, OR) paper saturated with 0.5 N NaOH and left at room temperature (RT) for 3 to 6 min to lyse the cells. Additional treatment of membranes was as described in the protocol provided by NEN Research Products.

2) DNA Hybridizations

Membranes were dried overnight before hybridizing to oligonucleotide probes prepared using a non-radioactive ECL™ 3'-oligolabelling and detection system from Amersham Life Sciences (Arlington Heights, IL). DNA labeling, prehybridization and hybridizations were performed according to manufacturer's protocols. After hybridization, membranes were washed twice at room temperature in 5 X SSC, 0.1% SDS (in a volume equivalent to 2 ml/cm^2 of membrane) for 5 min each followed by two washes at 50°C in 1X SSC, 0.1% SDS (in a volume

equivalent to 2 ml/cm^2 of membrane) for 15 min each. The hybridization signal was then generated and detected with Hyperfilm ECL™ (Amersham) according to manufacturer's protocols. Membranes were aligned to plates containing bacterial colonies from which colony lifts were performed and colonies corresponding to positive signals on X-ray were then isolated and propagated in LB broth. Plasmid DNA's were isolated from these cultures and analyzed by restriction enzyme digestions and by DNA sequencing.

B. Screening Genomic Libraries (Plaque Form)

1) λ Library Plating

E. coli XL1Blue-MRF' cells were grown overnight in LB medium (25 ml) containing 10 mM $MgSO_4$ and 0.2% maltose at 37°C, 250 rpm. Cells were then centrifuged (2,200 x g for 10 min) and resuspended in 0.5 volumes of 10 mM $MgSO_4$. 500 µl of this *E. coli* culture was mixed with a phage suspension containing 25,000 amplified lambda phage particles and incubated at 37°C for 15 min. To this mixture 6.5 ml of NZCYM top agarose (maintained at 60°C) (see Chart) was added and plated on 80 - 100 ml NCZYM agar (see Chart) present in a 150 mm petridish. Phage were allowed to propagate overnight at 37°C to obtain discrete plaques. After overnight growth plates were stored in a refrigerator for 1-2 hr before plaque lifts were performed.

2) **Plaque Lift and DNA Hybridizations**

Magna Lift™ nylon membranes (Micron Separations, Inc., Westborough, MA) were placed on the agar surface in complete contact with λ plaques and transfer of plaques to nylon membranes was allowed to proceed for 5 min at RT. After plaque transfer the membrane was placed on 2 sheets of Whatman 3M™ (Whatman, Hillsboro, OR) filter paper saturated with a 0.5 N NaOH, 1.0 M NaCl solution and left for 10 min at RT to denature DNA. Excess denaturing solution was removed by blotting briefly on dry Whatman 3M paper. Membranes were then transferred to 2 sheets of Whatman 3M™ paper saturated with 0.5 M Tris-HCl (pH 8.0), 1.5 M NaCl and left for 5 min to neutralize. Membranes were then briefly washed in 200 - 500 ml of 2 X SSC, dried by air and baked for 30 - 40 min at 80°C. The membranes were then probed with labelled DNA.

Membranes were prewashed with a 200 - 500 ml solution of 5 X SSC, 0.5% SDS, 1 mM EDTA (pH 8.0) for 1 - 2 hr at 42°C with shaking (60 rpm) to get rid of bacterial debris from the membranes. The membranes were prehybridized for 1 - 2 hr at 42°C with (in a volume equivalent to 0.125 - 0.25 ml/cm^2 of membrane) ECL Gold™ buffer (Amersham) containing 0.5 M NaCl and 5% blocking reagent. DNA fragments that were used as probes were purified from agarose gel using a QIAEX·II™ gel extraction kit (Qiagen Inc., Chatsworth, CA) according to manufacturers protocol and labeled using an Amersham ECL™ direct nucleic acid labeling kit (Amersham). Labeled DNA (5 - 10 ng/ml hybridization solution) was added to the prehybridized membranes and the hybridization was allowed to proceed overnight. The following day membranes were washed with shaking (60 rpm) twice at 42°C for 20 min each time in (in a volume equivalent to 2 ml/cm^2 of membrane) a buffer containing either 0.1 (high stringency) or 0.5 (low stringency) X SSC, 0.4% SDS and 360 g/l urea. This was followed by two 5 min washes at room temperature in (in a volume equivalent to 2 ml/cm^2 of membrane) 2 X SSC. Hybridization signals were generated using the ECL™ nucleic acid detection reagent and detected using Hyperfilm ECL™ (Amersham).

Agar plugs which contained plaques corresponding to positive signals on the X-ray film were taken from the master plates using the broad-end of Pasteur pipet. Plaques were selected by aligning the plates with the x-ray film. At this stage, multiple plaques were generally taken. Phage particles were eluted from the agar plugs by soaking in 1 ml SM buffer (Sambrook et al., *supra*) overnight. The phage eluate was then diluted and plated with freshly grown *E. coli* XL1Blue-MRF' cells to obtain 100 - 500 plaques per 85 mm NCZYM agar plate. Plaques were transferred to Magna Lift nylon membranes as before and probed again using the same probe. Single well-isolated plaques corresponding to signals on X - ray film were picked by removing agar plugs and eluting the phage by soaking overnight in 0.5 ml SM buffer.

C. Conversion of λ Clones to Plasmid Form

The lambda clones isolated were converted to plasmid form for further analysis. Conversion from the plaque to the plasmid form was accomplished by infecting the plaques into *E. coli* strain BM25.8. The *E. coli* strain was grown overnight at 31°C, 250 rpm in LB broth containing 10 mM $MgSO_4$ and 0.2% maltose until the OD_{600} reached 1.1 - 1.4. Ten milliliters of the vernight culture was removed and mixed with 100 µl of 1 M $MgCl_2$. A 200 µl volume of

cells was removed, mixed with 150 µl of eluted phage suspension and incubated at 31°C for 30 min. LB broth (400 µl) was added to the tube and incubation was continued at 31°C for 1 hr with shaking, 250 rpm. 1 - 10 µl of the infected cell suspension was plated on LB agar containing 100 µg/ml ampicillin (Sigma, St. Louis, MO). Well-isolated colonies were picked and grown overnight in 5 ml LB broth containing 100 µg/ml ampicillin at 37°C, 250 rpm. Plasmid DNA was isolated from these cultures and analyzed. To convert the λZAP Express™ vector to plasmid form *E. coli* strains XL1Blue-MRF' and XLOR were used. The conversion was performed according to the manufacturer's (Stratagene) protocols for single-plaque excision.

EXAMPLE 4

Transformation of *C. tropicalis* H5343 ura⁻

A. Transformation of *C. tropicalis* H5343 by Electroporation

5 ml of YEPD was inoculated with *C. tropicalis* H5343 *ura-* from a frozen stock and incubated overnight on a New Brunswick shaker at 30°C and 170 rpm. The next day, 10 µl of the overnight culture was inoculated into 100 ml YEPD and growth was continued at 30°C, 170 rpm. The following day the cells were harvested at an OD_{600} of 1.0 and the cell pellet was washed one time with sterile ice-cold water. The cells were resuspended in ice-cold sterile 35 % Polyethylene glycol (4,000 MW) to a density of $5x10^8$ cells/ml. A 0.1 ml volume of cells were utilized for each electroporation. The following electroporation protocol was followed: 1.0 µg of transforming DNA was added to 0.1 ml cells, along with 5 µg denatured, sheared calf thymus DNA and the mixture was allowed to incubate on ice for 15 min. The cell solution was then transferred to an ice-cold 0.2 cm electroporation cuvette, tapped to make sure the solution was on the bottom of the cuvette and electroporated. The cells were electroporated using an Invitrogen electroporator (Carlsbad, CA) at 450 Volts, 200 Ohms and 250 µF. Following electroporation, 0.9 ml SOS media (1M Sorbitol, 30% YEPD, 10 mM $CaCl_2$) was added to the suspension. The resulting culture was grown for 1 hr at 30°C, 170 rpm. Following the incubation, the cells were pelleted by centrifugation at 1500 x g for 5 min. The electroporated cells were resuspended in 0.2 ml of 1M sorbitol and plated on synthetic complete media minus uracil (SC - uracil) (Nelson, *supra*). In some cases the electroporated cells were

plated directly onto SC - uracil. Growth of transformants was monitored for 5 days. After three days, several transformants were picked and transferred to SC-uracil plates for genomic DNA preparation and screening.

B. Transformation of *C. tropicalis* Using Lithium Acetate

The following protocol was used to transform *C. tropicalis* in accordance with the procedures described in *Current Protocols in Molecular Biology*, Supplement 5, 13.7.1 (1989), incorporated herein by reference.

5 ml of YEPD was inoculated with *C. tropicalis* H5343 *ura-* from a frozen stock and incubated overnight on a New Brunswick shaker at 30°C and 170 rpm. The next day, 10 µl of the overnight culture was inoculated into 50 ml YEPD and growth was continued at 30°C, 170 rpm. The following day the cells were harvested at an OD_{600} of 1.0. The culture was transferred to a 50 ml polypropylene tube and centrifuged at 1000 X g for 10 min. The cell pellet was resuspended in 10 ml sterile TE (10mM Tris-Cl and 1mM EDTA, pH 8.0). The cells were again centrifuged at 1000 X g for 10 min and the cell pellet was resuspended in 10 ml of a sterile lithium acetate solution [LiAc (0.1 M lithium acetate, 10 mM Tris-Cl, pH 8.0, 1 mM EDTA)]. Following centrifugation at 1000 X g for 10 min., the pellet was resuspended in 0.5 ml LiAc. This solution was incubated for one hour at 30°C while shaking gently at 50 rpm. A 0.1 ml aliquot of this suspension was incubated with 5 µg of transforming DNA at 30°C with no shaking for 30 min. A 0.7 ml PEG solution (40 % wt/vol polyethylene glycol 3340, 0.1 M lithium acetate, 10 mM Tris-Cl, pH 8.0, 1 mM EDTA) was added and incubated at 30°C for 45 min. The tubes were then placed at 42°C for 5 min. A 0.2 ml aliquot was plated on synthetic complete media minus uracil (SC - uracil) (Kaiser et al. *Methods in Yeast Genetics*, Cold Spring Harbor Laboratory Press, USA, 1994, incorporated herein by reference). Growth of transformants was monitored for 5 days. After three days, several transformants were picked and transferred to SC-uracil plates for genomic DNA preparation and screening.

EXAMPLE 5

Plasmid DNA Isolation

Plasmid DNA were isolated from *E. coli* cultures using Qiagen plasmid isolation kit (Qiagen Inc., Chatsworth, CA) according to manufacturer's instructions.

EXAMPLE 6

DNA Sequencing and Analysis

DNA sequencing was performed at Sequetech Corporation (Mountain View, CA) using Applied Biosystems automated sequencer (Perkin Elmer, Foster City, CA). DNA sequences were analyzed with MacVector and GeneWorks software packages (Oxford Molecular Group, Campbell, CA).

EXAMPLE 7

PCR Protocols

PCR amplification was carried out in a Perkin Elmer Thermocycler using the Ampli*Taq*Gold enzyme (Perkin Elmer Cetus, Foster City, CA) kit according to manufacturer's specifications. Following successful amplification, in some cases, the products were digested with the appropriate enzymes and gel purified using QiaexII (Qiagen, Chatsworth, CA) as per manufacturer instructions. In specific cases the Ultma *Taq* polymerase (Perkin Elmer Cetus, Foster City, CA) or the Expand Hi-Fi *Taq* polymerase (Boehringer Mannheim, Indianapolis, IN) were used per manufacturer's recommendations or as defined in Table 3.

Table 3. PCR amplification conditions used with different primer combinations.

PRIMER COMBINATION	*Taq*	TEMPLATE DENATURING CONDITION	ANNEALING TEMP/TIME	EXTENSION TEMP/TIME	CYCLE Number
3674-41-1/ 41-2/ 41-4 + 3674-41-4	Ampli-*Taq* Gold	94 C/30 sec	55 C/30 sec	72 C/1 min	30
URA Primer 1a URA Primer 1b	Ampli-*Taq* Gold	95 C/1 min	70 C/1 min	72 C/2 min	35
URA Primer 2a URA Primer 2b	Ampli-*Taq* Gold	95 C/1 min	70 C/1 min	72 C/2 min	35
*CYP*2A#1 *CYP*2A#2	Ampli-*Taq* Gold	95 C/1 min	70 C/1 min	72 C/2 min	35
*CYP*3A#1 *CYP*3A#2	Ultma *Taq*	95 C/1 min	70 C/1 min	72 C/1 min	30
CPR B#1 *CPR* B#2	Expand Hi-Fi *Taq*	94 C/15 sec 94 C/15 sec	50 C/30 sec 50 C/30 sec	68 C/3 min 68 C/3 min +20 sec/cycle	10 15

CYP5A#1 *CYP5A#2*	Expand Hi-Fi *Taq*	94 C/15 s c 94 C/15 sec	50 C/30 sec 50 C/30 sec	68 C/3 min 68 C/3 min +20 sec/cycle	10 15

Table 4 below contains a list of primers (SEQ ID NOS: 1-35) used for PCR amplification to construct gene integration vectors or to generate probes for gene detection and isolation.

Table 4. Primer table for PCR amplification to construct gene integration vectors, to generate probes for gene isolation and detection and to obtain DNA sequence of constructs. (A- deoxyadenosine triphosphate [dATP], G- deoxyguanosine triphosphate [dGTP], C- deoxycytosine triphosphate [dCTP], T- deoxythymidine triphosphate [dTTP], Y- dCTP or dTTP, R- dATP or dGTP, W- dATP or dTTP, M- dATP or dCTP, N- dATP or dCTP or dGTP or dTTP).

Target gene(s)	Patent Primer Name	Lab Primer Name	Sequence (5' to 3')	PCR Product Size
CYP52A2A	CYP2A#1	3659-72M	*CCTTAATTAA*ATGCACGAAGCGGAGA TAAAAG (SEQ ID NO: 1)	2230 bp
	CYP2A#2	3659-72N	*CCTTAATTAA*GCATAAGCTTGCTCGAG TCT (SEQ ID NO: 2)	
CYP52A3A	CYP3A#1	3659-72O	*CCTTAATTAA*ACGCAATGGGAACATG GAGTG (SEQ ID NO: 3)	2154 bp
	CYP3A#2	3659-72P	*CCTTAATTAA*TCGCACTACGGTTATTG GTATCAG (SEQ ID NO: 4)	
CYP52A5A	CYP5A#1	3659-72K	*CCTTAATTAA*TCAAAGTACGTTCAGGC GG (SEQ ID NO: 5)	3298 bp
	CYP5A#2	3659-72L	*CCTTAATTAA*GGCAGACAACAACTTG GCAAAGTC (SEQ ID NO: 6)	
CPRB	CPRB#1	3698-20A	*CCTTAATTAA*GAGGTCGTTGGTTGAGT TTTC (SEQ ID NO: 7)	3266 bp
	CPRB#2	3698-20B	*CCTTAATTAA*TTGATAATGACGTTGCG GG (SEQ ID NO: 8)	
URA3A	URA Primer 1a	3698-7C	*AGGCGCGCC*GGAGTCCAAAAAGACC AACCTCTG (SEQ ID NO: 9)	956 bp
	URA Primer 1b	3698-7D	*CCTTAATTAA*TACGTGGATACCTTCAA GCAAGTG (SEQ ID NO: 10)	

URA3A	URA Primer 2a	3698-7A	*CCTTAATTAA*GCTCACGAGTTTTGGGA TTTTCGAG (SEQ ID NO: 11)	750 bp
	URA Primer 2b	3698-7B	*GGGTTTAAAC*CGCAGAGGTTGGTCTT TTTGGACTC (SEQ ID NO: 12)	
			GGGTTTAAAC - *Pme* I restriction site (SEQ ID NO: 13)	
			AGGCGCGCC - *Asc*I restriction site (SEQ ID NO: 14)	
			CCTTAATTAA - *Pac*I restriction site (SEQ ID NO: 15)	
CPR	FMN1	3674-41-1	TCYCAAACWGGTACWGCWGAA (SEQ ID NO: 16)	
CPR	FMN2	3674-41-2	GGTTTGGGTAAYTCWACTTAT (SEQ ID NO: 17)	
CPR	FAD	3674-41-3	CGTTATTAYTCYATTTCTTC (SEQ ID NO: 18)	
CPR	NADPH	3674-41-4	GCMACACCRGTACCTGGACC (SEQ ID NO: 19)	
CPR	PRK1.F3	PRK1.F3	ATCCCAATCGTAATCAGC (SEQ ID NO: 20)	
CPR	PRK1.F5	PRK1.F5	ACTTGTCTTCGTTTAGCA (SEQ ID NO: 21)	
CPR	PRK4.R20	PRK4.R20	CTACGTCTGTGGTGATGC (SEQ ID NO: 22)	
CYP	UCup1	UCup1	CGNGAYACNACNGCNGG (SEQ ID NO: 23)	
CYP	UCup2	UCup2	AGRGAYACNACNGCNGG (SEQ ID NO: 24)	
CYP	UCdown1	UCdown1	AGNGCRAAYTGYTGNCC (SEQ ID NO: 25)	
CYP	UCdown2	UCdown2	YAANGCRAAYTGYTGNCC (SEQ ID NO: 26)	
CYP	HemeB1	HemeB1	ATTCAACGGTGGTCCAAGAATCTGTT TGG (SEQ ID NO: 27)	
CYP	2,3,5P	2,3,5P	GAGCTATGTTGAGACCACAGTTTGC (SEQ ID NO: 28)	
CYP	2,3,5M	2,3,5M	CTTCAGTTAAAGCAAATTGTTTGGCC (SEQ ID NO: 29)	
pTriplEx vector	Triplex5'	Triplex5'	CTCGGGAAGCGCGCCATTGTGTTGG (SEQ ID NO: 30)	
pTriplEx vector	Triplex3'	Triplex3'	TAATACGACTCACTATAGGGCGAAT TGGC (SEQ ID NO: 31)	
CYP	Cyp52a	Cyp52a	TGRYTCAAACCATCTYTCTGG (SEQ ID NO: 32)	
CYP	Cyp52b	Cyp52b	GGACCGGCGTTAAAGGG (SEQ ID NO: 33)	
CYP	Cyp52c	Cyp52c	CATAGTCGWATYATGCTTAGACC (SEQ ID NO: 34)	
CYP	Cyp52d	Cyp52d	GGACCACCATTGAATGG (SEQ ID NO: 35)	

EXAMPLE 8

Yeast Colony PCR Procedure for Confirmation of Gene Integration into the Genome of *C. tropicalis*

Single yeast colonies were removed from the surface of transformation plates, suspended in 50 μl of spheroplasting buffer (50mM KCl, 10mM Tris-HCl, pH 8.3, 1.0 mg/ml Zymolyase, 5% glycerol) and incubated at 37°C for 30 min. Following incubation, the solution was heated for 10 min at 95°C to lyse the cells. Five μl of this solution was used as a template in PCR. Expand Hi-Fi *Taq* polymerase (Boehringer Mannheim, Indianapolis, IN) was used in PCR coupled with a gene-specific primer (gene to be integrated) and a *URA3* primer. If integration did occur, amplification would yield a PCR product of predicted size confirming the presence of an integrated gene.

EXAMPLE 9

Fermentation Method for Gene Induction Studies

A fermentor was charged with a semi-synthetic growth medium having the composition 75 g/l glucose (anhydrous), 6.7 g/l Yeast Nitrogen Base (Difco Laboratories), 3 g/l yeast extract, 3 g/l ammonium sulfate, 2 g/l monopotassium phosphate, 0.5 g/l sodium chloride. Components were made as concentrated solutions for autoclaving then added to the fermentor upon cooling: final pH approximately 5.2. This charge was inoculated with 5-10% of an overnight culture of *C. tropicalis* ATCC 20962 prepared in YM medium (Difco Laboratories) as described in the methods of Examples 17 and 20 of US Patent 5,254,466, which is incorporated herein by reference. *C. tropicalis* ATCC 20962 is a POX 4 and POX 5 disrupted *C. tropicalis* ATCC 20336. Air and agitation were supplied to maintain the dissolved oxygen at greater than about 40% of saturation versus air. The pH was maintained at about 5.0 to 8.5 by the addition of 5N caustic soda on pH control. Both a fatty acid feedstream (commercial oleic acid in this example) having a typical composition: 2.4% C_{14}; 0.7% $C_{14:1}$; 4.6% C_{16}; 5.7% $C_{16:1}$; 5.7% $C_{17:1}$; 1.0% C_{18}; 69.9% $C_{18:1}$; 8.8% $C_{18:2}$; 0.30% $C_{18:3;}$ 0.90% $C_{20:1}$ and a glucose co-substrate feed were added in a feedbatch mode beginning near the end of exponential growth. Caustic was added on pH control during the bioconversion of fatty acids to diacids to maintain the pH in the desired range. Typically, samples for gene induction studies were collected just prior to starting the fatty acid feed and over the first 10 hours of bioconversion. Determination of fatty acid and diacid

content was determined by a standard methyl ester protocol using gas liquid chromatography (GLC). Gene induction was measured using the QC-RT-PCR protocol described in this application.

EXAMPLE 10

RNA Preparation

The first step of this protocol involves the isolation of total cellular RNA from cultures of *C. tropicalis*. The cellular RNA was isolated using the Qiagen RNeasy Mini Kit (Qiagen Inc., Chatsworth, CA) as follows: 2 ml samples of *C. tropicalis* cultures were collected from the fermentor in a standard 2 ml screw capped Eppendorf style tubes at various times before and after the addition of the fatty acid or alkane substrate. Cell samples were immediately frozen in liquid nitrogen or a dry-ice/alcohol bath after their harvesting from the fermentor. To isolate total RNA from the samples, the tubes were allowed to thaw on ice and the cells pelleted by centrifugation in a microfuge for 5 minutes (min) at 4°C and the supernatant was discarded while keeping the pellet ice-cold. The microfuge tubes were filled 2/3 full with ice-cold Zirconia/Silica beads (0.5 mm diameter, Biospec Products, Bartlesville, OK) and the tube filled to the top with ice-cold RLT* lysis buffer (* buffer included with the Qiagen RNeasy Mini Kit). Cell rupture was achieved by placing the samples in a mini bead beater (Biospec Products, Bartlesville, OK) and immediately homogenized at full speed for 2.5 min. The samples were allowed to cool in a ice water bath for 1 minute and the homogenization/cool process repeated two more times for a total of 7.5 min homogenization time in the beadbeater. The homogenized cells samples were microfuged at full speed for 10 min and 700 µl of the RNA containing supernatant removed and transferred to a new eppendorf tube. 700 µl of 70% ethanol was added to each sample followed by mixing by inversion. This and all subsequent steps were performed at room temperature. Seven hundred microliters of each ethanol treated sample were transferred to a Qiagen RNeasy spin column, followed by centrifugation at 8,000 x g for 15 sec. The flow through was discarded and the column reloaded with the remaining sample (700 µl) and re-centrifuged at 8,000 x g for 15 sec. The column was washed once with 700 µl of buffer RW1*, and centrifuged at 8,000 x g for 15 sec and the flow through discarded. The column was placed in a new 2 ml collection tube and washed with 500 µl of RPE* buffer and the flow through discarded. The RPE* wash was repeated with centrifugation at 8,000 x g for 2 min and the flow through

discarded. The spin column was transferred to a new 1.5 ml collection tube and 100 µl of RNase free water added to the column followed by centrifugation at 8,000 x g for 15 seconds. An additional 75 µl of RNase free water was added to the column followed by centrifugation at 8,000 x g for 2 min. RNA eluted in the water flow through was collected for further purification.

The RNA eluate was then treated to remove contaminating DNA. Twenty microliters of 10X DNase I buffer (0.5 M tris (pH 7.5), 50 mM $CaCl_2$, 100 mM $MgCl_2$), 10 µl of RNase-free DNase I (2 Units/µl, Ambion Inc., Austin, Texas) and 40 units Rnasin (Promega Corporation, Madison, Wisconsin) were added to the RNA sample. The mixture was then incubated at 37°C for 15 to 30 min. Samples were placed on ice and 250 µl Lysis buffer RLT* and 250 µl ethanol (200 proof) added. The samples were then mixed by inversion. The samples were transferred to Qiagen RNeasy spin columns and centrifuged at 8,000 x g for 15 sec and the flow through discarded. Columns were placed in new 2 ml collection tubes and washed twice with 500 µl of RPE* wash buffer and the flow through discarded. Columns were transferred to new 1.5 ml eppendorf tubes and RNA was eluated by the addition of 100 µl of DEPC treated water followed by centrifugation at 8,000 x g for 15 sec. Residual RNA was collected by adding an additional 50 µl of RNase free water to the spin column followed by centrifugation at full speed for 2 min. 10 µl of the RNA preparation was removed and quantified by the ($A_{260/280}$) method. RNA was stored at
-70°C. Yields were found to be 30-100 µg total RNA per 2.0 ml of fermentation broth.

EXAMPLE 11

Quantitative Competitive Reverse Transcription Polymerase Chain Reaction (QC-RT-PCR) Protocol

QC-RT-PCR is a technique used to quantitate the amount of a specific RNA in a RNA sample. This technique employs the synthesis of a specific DNA molecule that is complementary to an RNA molecule in the original sample by reverse transcription and its subsequent amplification by polymerase chain reaction. By the addition of various amounts of a competitor RNA molecule to the sample one can determine the concentration of the RNA molecule of interest (in this case the mRNA transcripts of the *CYP* and *CPR* genes). The levels of specific mRNA transcripts were assayed over time in response to the addition of fatty acid

and/or alkane substrates to the growth medium of fermentation grown *C. tropicalis* cultures for the identification and characterization of the genes involved in the oxidation of these substrates. This approach can be used to identify the *CYP* and *CPR* genes involved in the oxidation of any given substrate based upon their transcriptional regulation.

A. Primer Design

The first requirement for QC-RT-PCR is the design of the primer pairs to be used in the reverse transcription and subsequent PCR reactions. These primers need to be unique and specific to the gene of interest. As there is a family of genetically similar *CYP* genes present in *C. tropicalis* 20336, care had to be taken to design primer pairs that would be discriminating and only amplify the gene of interest, in this example the *CYP52A5* gene. In this manner, unique primers directed to substantially non-homologous (aka variable) regions within target members of a gene family are constructed. What constitutes substantially non-homologous regions is determined on a case by case basis. Such unique primers should be specific enough to anneal the non-homologous region of the target gene without annealing to other non-target members of the gene family. By comparing the known sequences of the members of a gene family, non-homologous regions are identified and unique primers are constructed which will anneal to those regions. It is contemplated that non-homologous regions herein would typically exhibit less than about 85% homology but can be more homologous depending on the positions which are conserved and stringency of the reaction. After conducting PCR, it may be helpful to check the reaction product to assure it represents the unique target gene product. If not, the reaction conditions can be altered in terms of stringency to focus the reaction to the desired target. Alternatively a new primer or new non-homologous region can be chosen. Due to the high level of homology between the genes of the *CYP52A* family, the most variable 5 prime region of the *CYP52A5* coding sequence was targeted for the design of the primer pairs. In Figure 3, a portion of the 5 prime coding region for the *CYP52A5*A (SEQ ID NO: 36) allele of *C. tropicalis* 20336 is shown. The boxed sequences in Figure 3 are the sequences of the forward and backwards primers (SEQ ID NOS: 47 and 48) used to quantitate expression of both alleles of this gene. The actual reverse primer (SEQ ID NO: 48) contains one less adenine than that shown in Figure 3. Primers used to measure the expression of specific *C. tropicalis* 20336 genes using the QC-RT-PCR protocol are listed in Table 5 (SEQ ID NOS: 37-58).

Table 5. Primer used to measure *C. tropicalis* gene expression in the QC-RT-PCR reactions.

Primer Name	Direction	Target	Sequence
3737-89F	F	*CYP52A1A*	CCGATGAAGTTTTCGACGAGTACCC (SEQ ID NO: 37)
3737-89B	B	*CYP52A1A*	AAGGCTTTAACGTGTCCAATCTGGTC (SEQ ID NO: 38)
alk2aF1	F	*CYP52A2A*	ATTATCGCCACATACTTCACCAAATGG (SEQ ID NO: 39)
alk2aB5	B	*CYP52A2A*	CGAGATCGTGGATACGCTGGAGTG (SEQ ID NO: 40)
7581-178-3	F	*CYP52A3A*	GCCACTCGGTAACTTTGTCAGGGAC (SEQ ID NO: 41)
7581-178-4	B	*CYP52A3A*	CATTGAACTGAGTAGCCAAAACAGCC (SEQ ID NO: 42)
3737-50F	F	*CYP52A3A & CYP52A3B*	CCTACGTTTGGTATCGCTACTCCGTTG (SEQ ID NO: 43)
3737-50B	B	*CYP52A3A & CYP52A3B*	TTTCCAGCCAGCACCGTCCAAG (SEQ ID NO: 44)
3737-175F	F	*CYP52D4A*	GCAGAGCCGATCTATGTTGCGTCC (SEQ ID NO: 45)
3737-175B	B	*CYP52D4A*	TCATTGAATGCTTCCAGGAACCTCG (SEQ ID NO: 46)
7581-97-F	F	*CYP52A5A& CYP52A5B*	AAGAGGGCAGGGCTCAAGAG (SEQ ID NO: 47)
7581-97-M	B	*CYP52A5A& CYP52A5B*	TCCATGTGAAGATCCCATCAC (SEQ ID NO: 48)
4P-2	F	*CYP52A8A*	CTTGAAGGCCGTGTTGAACG (SEQ ID NO: 49)
4M-1	B	*CYP52A8A*	CAGGATTTGTCTGAGTTGCCG (SEQ ID NO: 50)
3737-52F	F	*POX4A & POX4B*	CCATTGCCTTGAGATACGCCATTGGTAG (SEQ ID NO: 51)
3737-52B	B	*POX4A & POX4B*	AGCCTTGGTGTCGTTCTTTTCAACGG (SEQ ID NO: 52)
3737-53F	F	*POX5A*	TTGGGTTTGTTTGTTTCCTGTGTCCG (SEQ ID NO: 53)
3737-53B	B	*POX5A*	CCTTTGACCTTCAATCTGGCGTAGACG (SEQ ID NO: 54)
F33	F	*CPRA*	GGTTTGCTGAATACGCTGAAGGTGATG (SEQ ID NO: 55)
B63	B	*CPRA*	TGGAGCTGAACAACTCTCTCGTCTCGG (SEQ ID NO: 56)
3737-133F	F	*CPRA & CPRB*	TTCCTCAACACGGACAGCGG (SEQ ID NO: 57)
3737-133B	B	*CPRA & CPRB*	AGTCAACCAGGTGTGGAACTCGTC (SEQ ID NO: 58)

F=Forward B=Backward

B. Design and Synthesis of the Competit r DNA Template

The competitor RNA is synthesized *in vitro* from a competitor DNA template that has the T7 polymerase promoter and preferably carries a small deletion of e.g., about 10 to 25 nucleotides relative to the native target RNA sequence. The DNA template for the *in-vitro* synthesis of the competitor RNA is synthesized using PCR primers that are between 46 and 60 nucleotides in length. In this example, the primer pairs for the synthesis of the *CYP52A5* competitor DNA are shown in Tables 6 and 7 (SEQ ID NOS: 59 AND 60).

Table 6. Forward and Reverse primers used to synthesize the competitor RNA template for the QC-RT-PCR measurement of *CYP52A5A* gene expression.

Forward Primer	*CYP52A5*A	GGATCCTAATACGACTCACTATAGGGAGGA AGAGGGCAGGGCTCAAGAG (SEQ ID NO: 59)
Reverse Primer	*CYP52A5*A	TCCATGTGAAGATCCCATCACGAGTGTGCC TCTTGCCCAAAG (SEQ ID NO: 60)

Table 7. Primers for the synthesis of the QC-RT-PCR competitor RNA templates

Primer Name	Direction	Target	Sequence 5'-3'
3737-89C	F	*CYP52A1A*	GGATCCTAATACGACTCACTATAGGGAGGCCGATG AAGTTTTCGACGAGTACCC (SEQ ID NO: 61)
3737-89D	B	*CYP52A1A*	AAGGCTTTAACGTGTCCAATCTGGTC AACATAGCTCTGGAGTGCTTCCAACC (SEQ ID NO: 62)
7581-137-A	F	*CYP52A2A*	GGATCCTAATACGACTCACTATAGGGAGGATTATC GCCACATACTTCACCAAATGG (SEQ ID NO: 63)
7581-137-B	B	*CYP52A2A*	CGAGATCGTGGATACGCTGGAGTGCGTCGCTCTTC TTCTTCAACAATTCAAG (SEQ ID NO: 64)
7581-137-D	B	*CYP52A3A*	CATTGAACTGAGTAGCCAAAACAGCCCATGGTTTC AATCAATGGGAGGC (SEQ ID NO: 65)
7581-137-C	F	*CYP52A3A*	GGATCCTAATACGACTCACTATAGGGAGGGCCACT CGGTAACTTTGTCAGGGAC (SEQ ID NO: 66)

3737-50-D	F	*CYP52A3A & CYP52A3B*	GGATCCTAATACGACTCACTATAGGGAGGCCTACG TTTGGTATCGCTACTCCGTTG (SEQ ID NO: 67)
3737-50-C	B	*CYP52A3A & CYP52A3B*	TTTCCAGCCAGCACCGTCCAAGCAACAAGGAGTAC AAGAAATCGTGTC (SEQ ID NO: 68)
3737-175C	F	*CYP52D4A*	GGATCCTAATACGACTCACTATAGGGAGGGCAGAG CCGATCTATGTTGCGTCC (SEQ ID NO: 69)
3737-175D	B	*CYP52D4A*	TCATTGAATGCTTCCAGGAACCTCGCCACATCCATC GAGAACCGG (SEQ ID NO: 70)
7581-97-A	F	*CYP52A5A & CYP52A5B*	GGATCCTAATACGACTCACTATAGGGAGGAAGAGG GCAGGGCTCAAGAG (SEQ ID NO: 59)
7581-97-B	B	*CYP52A5A & CYP52A5B*	TCCATGTGAAGATCCCATCACGAGTGTGCCTCTTGC CCAAAG (SEQ ID NO: 60)
4P-2/T7	F	*CYP52A8A*	GGATCCTAATACGACTCACTATAGGGAGGCTTGAA GGCCGTGTTGAACG (SEQ ID NO: 71)
4M-3/4M-1	B	*CYP52A8A*	CAGGATTTGTCTGAGTTGCCGCCTGATCAAGATAG GATCCTTGCCG (SEQ ID NO: 72)
3737-26-D	F	*CPRA*	GGATCCTAATACGACTCACTATAGGGAGGGGTTTG CTGAATACGCTGAAGGTGATG (SEQ ID NO: 73)
3737-26-C	B	*CPRA*	TGGAGCTGAACAACTCTCTCGTCTCGGGTGGTCGA ATGGACCCTTGGTCAAG (SEQ ID NO: 74)
3737-133C	F	*CPRA & CPRB*	GGATCCTAATACGACTCACTATAGGGAGGTTCCTC AACACGGACAGCGG (SEQ ID NO: 75)
3737-133D	B	*CPRA & CPRB*	AGTCAACCAGGTGTGGAACTCGTCGGTGGCAACAA TGAAAAACACCAAG (SEQ ID NO: 76)
3737-52-C	F	*POX4A & POX4B*	GGATCCTAATACGACTCACTATAGGGAGGCCATTG CCTTGAGATACGCCATTGGTAG (SEQ ID NO: 77)
3737-52-D	B	*POX4A & POX4B*	AGCCTTGGTGTCGTTCTTTTCAACGGAAGGTGGTCT CGATGGTGTGTTCAACC (SEQ ID NO: 78)
3737-53-C	F	*POX5A*	GGATCCTAATACGACTCACTATAGGGAGGTTGGGT TTGTTTGTTTCCTGTGTCCG (SEQ ID NO: 79)
3737-53-D	B	*POX5A*	CCTTTGACCTTCAATCTGGCGTAGACGCAGCACCA CCGATCCACCACTTG (SEQ ID NO: 80)

F=Forward B=Backword

The forward primer (SEQ ID NO: 59) contains the T7 promoter consensus sequence "GGATCCTAATACGA CTCACTATAGGG AGG" fused to the primer 7581-97-F sequence (SEQ ID NO: 47). The Reverse Primer (SEQ ID NO: 60) contains the sequence of primer 7581-97M (SEQ ID NO: 48) followed by the 20 bases of upstream sequence with a 18 base pair deletion between the two blocks of the *CYP52A5* sequence. The forward primer was used with the corresponding reverse primer to synthesize the competitor DNA template. The primer pairs were combined in a standard *Taq* Gold polymerase PCR reaction according to the manufacturer's recommended conditions (Perkin-Elmer/Applied Biosystems, Foster City, CA). The PCR reaction mix contained a final concentration of 250 nM each primer and 10 ng *C. tropicalis* chromosomal DNA for template. The reaction mixture was placed in a thermocycler for 25 to 35 cycles using the highest annealing temperature possible during the PCR reactions to assure a homogeneous PCR product (in this case 62°C). The PCR products were either gel purified or filtered purified to remove un-incorporated nucleotides and primers. The competitor template DNA was then quantified using the ($A_{260/280}$) method. Primers used in QC-RT-PCR experiments for the synthesis of various competitive DNA templates are listed in Table 7 (SEQ ID NOS: 61-80).

C. Synthesis of the Competitor RNA

Competitor template DNA was transcribed *In-Vitro* to make the competitor RNA using the Megascript T7 kit from Ambion Biosciences (Ambion Inc., Austin, Texas). 250 nanograms (ng) of competitor DNA template and the *in-vitro* transcription reagents are mixed according to the directions provided by the manufacturer. The reaction mixture was incubated for 4 hours at 37°C. The resulting RNA preparations were then checked by gel electrophoresis for the conditions giving the highest yields and quality of competitor RNA. This often required optimization according to the manufacturer's specifications. The DNA template was then removed using DNase I as described in the Ambion kit. The RNA competitor was then quantified by the ($A_{260/280}$) method. Serial dilution's of the RNA (1 ng/µl to 1 femtogram (fg)/µl) were made for use in the QC-RT-PCR reactions and the original stocks stored at -70°C.

D. QC-RT-PCR Reactions

QC-RT-PCR reactions were performed using rTth polymerase from Perkin-Elmer(Perkin-Elmer/Applied Biosystems, Foster City, CA) according to the manufacturer's recommended conditions. The reverse transcription reaction was performed in a 10 µl volume with a final concentrations of 200 µM for each dNTP, 1.25 units rTth polymerase, 1.0 mM $MnCl_2$, 1X of the 10X buffer supplied with the Enzyme from the manufacturer, 100 ng of total RNA isolated from a fermentor grown culture of *C. tropicalis* and 1.25 µM of the appropriate reverse primer. To quantitate *CYP52A5* expression in *C. tropicalis* an appropriate reverse primer was 7581-97M (SEQ ID NO: 48). Several reaction mixes were prepared for each RNA sample characterized. To quantitate *CYP52A5* expression a series of 8 to 12 of the previously described QC-RT-PCR reaction mixes were aliquoted to different reaction tubes. To each tube 1 µl of a serial dilution containing from 100 pg to100 fg *CYP52A5* competitor RNA per µl was added bringing the final reaction mixtures up to the final volume of 10 µl. The QC-RT-PCR reaction mixtures were mixed and incubated at 70°C for 15 min according to the manufacturer's recommended times for reverse transcription to occur. At the completion of the 15 minute incubation, the sample temperature was reduced to 4°C to stop the reaction and 40 µl of the PCR reaction mix added to the reaction to bring the total volume up to 50 µl. The PCR reaction mix consists of an aqueous solution containing 0.3125 µM of the forward primer 7581-97F (SEQ ID NO: 47), 3.125 mM $MgCl_2$ and 1X chelating buffer supplied with the enzyme from Perkin-Elmer. The reaction mixtures were placed in a thermocycler (Perkin-Elmer GeneAmp PCR System 2400, Perkin-Elmer/Applied Biosystems, Foster City, CA) and the following PCR cycle performed: 94°C for 1 min. followed by 94°C for 10 seconds followed by 58°C for 40 seconds for 17 to 22 cycles. The PCR reaction was completed with a final incubation at 58°C for 2 min followed by 4°C. In some reactions where no detectable PCR products were produced the samples were returned the thermocycler for additional cycles, this process was repeated until enough PCR products were produced to quantify using HPLC. The number of cycles necessary to produce enough PCR product is a function of the amount of the target mRNA in the 100 ng of total cellular RNA. In cultures where the *CYP52A5* gene is highly expressed there is sufficient *CYP52A5* mRNA message present and less PCR cycles (≤17) are required to produce quantifiable amount of PCR product. The lower the concentrations of the target mRNA present the more PCR cycles are required to produce a detectable amount of product. These QC-RT-

PCR procedures were applied to all the target genes listed in Table 5 using the respective primers indicated therein.

E. HPLC Quantification

Upon completion of the QC-RT-PCR reactions the samples were analyzed and quantitated by HPLC. Five to fifteen microliters of the QC-RT-PCR reaction mix was injected into a Waters Bio-Compatible 625 HPLC with an attached Waters 484 tunable detector. The detector was set to measure a wave length of 254 nm. The HPLC contained a Sarasep brand DNASep™ column (Sarasep, Inc., San Jose, CA) which was placed within the oven and the temperature set for 52 °C. The column was installed according to the manufacturer's recommendation of having 30 cm. of heated PEEK tubing installed between the injector and the column. The system was configured with a Sarasep brand Guard column positioned before the injector. In addition, there was a 0.22 μm filter disk just before the column, within the oven. Two Buffers were used to create an elution gradient to resolve and quantitate the PCR products from the QC-RT-PCR reactions. Buffer-A consists of 0.1 M tri-ethyl ammonium acetate (TEAA) and 5% acetonitrile (volume to volume). Buffer-B consists of 0.1 M TEAA and 25% acetonitrile (volume to volume). The QC-RT-PCR samples were injected into the HPLC and the linear gradient of 75% buffer-A/ 25% buffer-B to 45% buffer-A/ 55% B was run over 6 min at a flow rate of 0.85 ml per minute. The QC-RT-PCR product of the competitor RNA being 18 base pairs smaller is eluted from the HPLC column before the QC-RT-PCR product from the *CYP52A5* mRNA(U). The amount of the QC-RT-PCR products are plotted and quantitated with an attached Waters Corporation 745 data module. The log ratios of the amount of *CYP52A5* mRNA QC-RT-PCR product (U) to competitor QC-RT-PCR product (C), as measured by peak areas, was plotted and the amount of competitor RNA required to equal the amount of *CYP52A5* mRNA product determined. In the case of each of the target genes listed in Table 5, the competitor RNA contained fewer base pairs as compared to the native target mRNA and eluted before the native mRNA in a manner similar to that demonstrated by *CYP52A5*. HPLC quantification of the genes was conducted as above.

EXAMPLE 12

Evaluation of New Strains in Shake Flasks

The *CYP* and *CPR* amplified strains such as strains HDC10, HDC15, HDC20 and HDC23 (Table 1) and H5343 were evaluated for diacid production in shake flasks. A single colony for each strain was transferred from a YPD agar plate into 5 ml of YPD broth and grown overnight at 30°C, 250 rpm. An inoculum was then transferred into 50 ml of DCA2 medium (Chart) and grown for 24 h at 30°C, 300 rpm. The cells were centrifuged at 5000 rpm for 5 min and resuspended in 50 ml of DCA3 medium (Chart) and grown for 24 h at 30°C, 300 rpm. 3% oleic acid w/v was added after 24 h growth in DCA3 medium and the cultures were allowed to bioconvert oleic acid for 48 h. Samples were harvested and the diacid and monoacid concentrations were analyzed as per the scheme given in Figure 35. Each strain was tested in duplicate and the results shown in Table 8 represent the average value from two flasks.

Table 8. Bioconversion of oleic acid by different recombinant strains of *Candida tropicalis*

Strain	Conversion to Oleic diacid (%)	Specific Conversion (g diacid/g biomass
H5343	41.9	0.53
HDC 10-2	50.5	0.85
HDC 15	54.4	0.85
HDC 20-1	45.1	0.72
HDC 20-2	45.3	0.58
HDC 23-2	55.2	0.84
HDC 23-3	58.8	0.89

EXAMPLE 13

Cloning and Characterization of *C. tropicalis* 20336 Cytochrome P450 Monooxygenase (*CYP*) and Cytochrome P450 NADPH Oxidoreductase (*CPR*) Genes

To clone *CYP* and *CPR* genes several different strategies were employed. Available CYP amino acid sequences were aligned and regions of similarity were observed (Figure 4). These regions corresponded to described conserved regions seen in other cytochrome P450 families (Goeptar et al., *supra* and Kalb et al. *supra*). Proteins from eight eukaryotic

cytochrome P450 families share a segmented region of sequence similarity. One region corresponded to the HR2 domain containing the invariant cysteine residue near the carboxyl terminus which is required for heme binding while the other region corresponded to the central region of the I helix thought to be involved in substrate recognition (Figure 4). Degenerate oligonucleotide primers corresponding to these highly conserved regions of the *CYP52* gene family present in *Candida maltosa* and *Candida tropicalis* ATCC 750 were designed and used to amplify DNA fragments of *CYP* genes from *C. tropicalis* 20336 genomic DNA. These discrete PCR fragments were then used as probes to isolate full-length *CYP* genes from the *C. tropicalis* 20336 genomic libraries. In a few instances oligonucleotide primers corresponding to highly conserved regions were directly used as probes to isolate full-length *CYP* genes from genomic libraries. In the case of *CPR* a heterologous probe based upon the known DNA sequence for the *CPR* gene from *C. tropicalis* 750 was used to isolate the *C. tropicalis* 20336 *CPR* gene.

A. Cloning of the *CPR* Gene from *C. tropicalis* 20336

1) Cloning of the *CPRA* Allele

Approximately 25,000 phage particles from the first genomic library of *C. tropicalis* 20336 were screened with a 1.9 kb *Bam*HI-*Nde*I fragment from plasmid pCU3RED (See Picattagio et al., Bio/Technology 10:894-898 (1992), incorporated herein by reference) containing most of the *C. tropicalis* 750 *CPR* gene. Five clones that hybridized to the probe were isolated and the plasmid DNA from these lambda clones was rescued and characterized by restriction enzyme analysis. The restriction enzyme analysis suggested that all five clones were identical but it was not clear that a complete *CPR* gene was present.

PCR analysis was used to determine if a complete *CPR* gene was present in any of the five clones. Degenerate primers were prepared for highly conserved regions of known *CPR* genes (See Sutter et al., *J. Biol. Chem.* 265:16428-16436 (1990), incorporated herein by reference) (Figure 4). Two Primers were synthesized for the FMN binding region (FMN1, SEQ ID NO: 16 and FMN2, SEQ ID NO: 17). One primer was synthesized for the FAD binding region (FAD, SEQ ID NO: 18), and one primer for the NADPH binding region (NADPH, SEQ ID NO: 19) (Table 4). These four primers were used in PCR amplification experiments using as a template plasmid DNA isolated from four of the five clones described above. The FMN (SEQ

ID NOS: 16 and 17) and FAD (SEQ ID NO: 18) primers served as forward primers and the NADPH primer (SEQ ID NO: 19) as the reverse primer in the PCR reactions. When different combinations of forward and reverse primers were used, no PCR products were obtained from any of the plasmids. However, all primer combinations amplified expected size products with a plasmid containing the *C. tropicalis* 750 *CPR* gene (positive control). The most likely reason for the failure of the primer pairs to amplify a product, was that all four of clones contained a truncated *CPR* gene. One of the four clones (pHKM1) was sequenced using the Triplex 5' (SEQ ID NO: 30) and the Triplex 3' (SEQ ID NO: 31) primers (Table 4) which flank the insert and the multiple cloning site on the cloning vector, and with the degenerate primer based upon the NADPH binding site described above. The NADPH primer (SEQ ID NO: 19) failed to yield any sequence data and this is consistent with the PCR analysis. Sequences obtained with Triplex primers were compared with *C. tropicalis* 750 *CPR* sequence using the MacVector™ program (Oxford Molecular Group, Campbell, CA). Sequence obtained with the Triplex 3' primer (SEQ ID NO: 31) showed similarity to an internal sequence of the *C. tropicalis* 750 *CPR* gene confirming that pHKM1 contained a truncated version of a 20336 *CPR* gene. pHKM1 had a 3.8 kb insert which included a 1.2 kb coding region of the *CPR* gene accompanied by 2.5 kb of upstream DNA (Figure 5). Approximately 0.85 kb of the 20336 *CPR* gene encoding the C-terminal portion of the *CPR* protein is missing from this clone.

Since the first Clontech library yielded only a truncated *CPR* gene, the second library prepared by Clontech was screened to isolate a full-length *CPR* gene. Three putative *CPR* clones were obtained. The three clones, having inserts in the range of 5-7 kb, were designated pHKM2, pHKM3 and pHKM4. All three were characterized by PCR using the degenerate primers described above. Both pHKM2 and pHKM4 gave PCR products with two sets of internal primers. pHKM3 gave a PCR product only with the FAD (SEQ ID NO: 18) and NADPH (SEQ ID NO: 19) primers suggesting that this clone likely contained a truncated *CPR* gene. All three plasmids were partially sequenced using the two Triplex primers and a third primer whose sequence was selected from the DNA sequence near the truncated end of the *CPR* gene present in pHKM1. This analysis confirmed that both pHKM2 & 4 have sequences that overlap pHKM1 and that both contained the 3' region of *CPR* gene that is missing from pHKM1. Portions of inserts from pHKM1 and pHKM4 were sequenced and a full-length *CPR* gene was identified. Based on the DNA sequence and PCR analysis, it was concluded that

pHKM1 contained the putative promoter region and 1.2 kb of sequence encoding a portion (5' end) of a *CPR* gene. pHKM4 had 1.1 kb of DNA that overlapped pHKM1 and contained the remainder (3' end) of a *CPR* gene along with a downstream untranslated region (Figure 6). Together these two plasmids contained a complete *CPRA* gene with an upstream promoter region. *CPRA* is 4206 nucleotides in length (SEQ ID NO: 81) and includes a regulatory region and a protein coding region (defined by nucleotides 1006-3042) which is 2037 base pairs in length and codes for a putative protein of 679 amino acids (SEQ ID NO: 83) (Figures 13 and 14). In Figure 13, the asterisks denote conserved nucleotides between *CPRA* and *CPRB*, bold denotes protein coding nucleotides, and the start and stop codons are underlined. The *CPRA* protein, when analyzed by the protein alignment program of the GeneWorks™ software package (Oxford Molecular Group, Campbell, CA), showed extensive homology to *CPR* proteins from *C. tropicalis* 750 and *C. maltosa*.

2) Cloning of the *CPRB* Allele

To clone the second *CPRB* allele, the third genomic library, prepared by Henkel, was screened using DNA fragments from pHKM1 and pHKM4 as probes. Five clones were obtained and these were sequenced with the three internal primers used to sequence *CPRA*. These primers were designated PRK1.F3 (SEQ ID NO: 20) , PRK1.F5 (SEQ ID NO: 21) and PRK4.R20 (SEQ ID NO: 22) (Table 4). and the two outside primers (M13 -20 and T3 [Stratagene]) for the polylinker region present in the pBK-CMV cloning vector. Sequence analysis suggested that four of these clones, designated pHKM5 to 8, contained inserts which were identical to the *CPRA* allele isolated earlier. All four seemed to contain a full length *CPR* gene. The fifth clone was very similar to the *CPRA* allele, especially in the open reading frame region where the identity was very high. However, there were significant differences in the 5' and 3' untranslated regions. This suggested that the fifth clone was the allele to *CPRA*. The plasmid was designated pHKM9 (Figure 7) and a 4.14 kb region of this plasmid was sequenced and the analysis of this sequence confirmed the presence of the *CPRB* allele (SEQ ID NO: 82), which includes a regulatory region and a protein coding region (defined by nucleotides 1033-3069) (Figure 13). The amino acid sequence of the *CPRB* protein is set forth in SEQ ID NO: 84 (Figure 14).

B. Cloning of *C. tropicalis* 20336 (*CYP*) Genes

1) Cloning of *CYP52A2A*, *CYP52A3A & 3B* and *CYP52A5A & 5B*

Clones carrying *CYP52A2A*, *A3A*, *A3B*, *A5A* and *A5B* genes were isolated from the first and second Clontech genomic libraries using an oligonucleotide probe (HemeB1, SEQ ID NO: 27) whose sequence was based upon the amino acid sequence for the highly conserved heme binding region present throughout the *CYP52* family. The first and second libraries were converted to the plasmid form and screened by colony hybridizations using the HemeB1 probe (SEQ ID NO: 27) (Table 4). Several potential clones were isolated and the plasmid DNA was isolated from these clones and sequenced using the HemeB1 oligonucleotide (SEQ ID NO: 27) as a primer. This approach succeeded in identifying five *CYP52* genes. Three of the *CYP* genes appeared unique, while the remaining two were classified as alleles. Based upon an arbitrary choice of homology to *CYP52* genes from *Candida maltosa*, these five genes and corresponding plasmids were designated *CYP52A2A* (pPA15 [Figure 26]), *CYP52A3A* (pPA57 [Figure 29]), *CYP52A3B* (pPA62 [Figure 30]), *CYP52A5A* (pPAL3 [Figure 31]) and *CYP52A5B* (pPA5 [Figure 32]). The complete DNA sequence including regulatory and protein coding regions of these five genes was obtained and confirmed that all five were *CYP52* genes (Figure 15). In Figure 15, the asterisks denote conserved nucleotides among the *CYP* genes. Bold indicates the protein coding nucleotides of the *CYP* genes, and the start and stop codons are underlined. The *CYP52A2A* gene as represented by SEQ ID NO: 86 has a protein coding region defined by nucleotides 1199-2767 and the encoded protein has an amino acid sequence as set forth in SEQ ID NO: 96. The *CYP52A3A* gene as represented by SEQ ID NO: 88 has a protein encoding region defined by nucleotides 1126-2748 and the encoded protein has an amino acid sequence as set forth in SEQ ID NO: 98. The *CYP52A3B* gene as represented by SEQ ID NO: 89 has a protein coding defined by nucleotides 913-2535 and the encoded protein has an amino acid sequence as set forth in SEQ ID NO: 99. The *CYP52A5A* gene as represented by SEQ ID NO: 90 has a protein coding region defined by nucleotides 1103-2656 and the encoded protein has an amino acid sequence as set forth in SEQ ID NO: 100. The *CYP52A5B* gene as represented by SEQ ID NO: 91 has a protein coding region defined by nucleotides 1142-2695 and the encoded protein has an amino acid sequence as set forth in SEQ ID NO: 101.

2) Cl ning of *CYP52A1A* and *CYP52A8A*

CYP52A1A and *CYP52A8A* genes were isolated from the third genomic library using PCR fragments as probes. The PCR fragment probe for *CYP52A1* was generated after PCR amplification of 20336 genomic DNA with oligonucleotide primers that were designed to amplify a region from the Helix I region to the HR2 region using all available *CYP52* genes from National Center for Biotechnology Information. Degenerate forward primers UCup1 (SEQ ID NO: 23) and UCup2 (SEQ ID NO: 24) were designed based upon an amino acid sequence (-RDTTAG-) from the Helix I region (Table 4). Degenerate primers UCdown1 (SEQ ID NO: 25) and UCdown2 (SEQ ID NO: 26) were designed based upon an amino acid sequence (-GQQFAL-) from the HR2 region (Table 4). For the reverse primers, the DNA sequence represents the reverse complement of the corresponding amino acid sequence. These primers were used in pairwise combinations in a PCR reaction with Stoffel *Taq* DNA polymerase (Perkin-Elmer Cetus, Foster City, CA) according to the manufacturer's recommended procedure. A PCR product of approximately 450 bp was obtained. This product was purified from agarose gel using Gene-clean™ (Bio 101, LaJolla, CA) and ligated to the pTAG™ vector (Figure 17) (R&D systems, Minneapolis, MN) according to the recommendations of the manufacturer. No treatment was necessary to clone into pTAG because it employs the use of the TA cloning technique. Plasmids from several transformants were isolated and their inserts were characterized. One plasmid contained the PCR clone intact. The DNA sequence of the PCR fragment (designated 44*CYP*3, SEQ ID NO: 107) shared homology with the DNA sequences for the *CYP52A1* gene of *C. maltosa* and the *CYP52A3* gene of *C. tropicalis 750.* This fragment was used as a probe in isolating the *C. tropicalis* 20336 *CYP52A1* homolog. The third genomic library was screened using the 44*CYP*3 PCR probe (SEQ ID NO: 107) and a clone (pHKM11) that contained a full-length *CYP52* gene was obtained (Figure 8). The clone contained a gene having regulatory and protein coding regions. An open reading frame of 1572 nucleotides encoded a *CYP52* protein of 523 amino acids (Figures 15 and 16). This *CYP52* gene was designated *CYP52A1A* (SEQ ID NO: 85) since its putative amino acid sequence (SEQ ID NO: 95) was most similar to the *CYP52A1* protein of *C. maltosa*. The protein coding region of the *CYP52A1A* gene is defined by nucleotides 1177-2748 of SEQ ID NO: 85.

A similar approach was taken to clone *CYP52A8A*. A PCR fragment probe for *CYP52A8* was generated using primers for highly conserved sequences of *CYP52A3*, *CYP52A2*

and *CYP52A5* genes of *C. tropicalis 750*. The reverse primer (primer 2,3,5,M) (SEQ ID NO: 29) was designed based on the highly conserved heme binding region (Table 4). The design of the forward primer (primer 2,3,5,P) (SEQ ID NO: 28) was based upon a sequence conserved near the N-terminus of the *CYP52A3*, *CYP52A2* and *CYP52A5* genes from *C. tropicalis 750* (Table 4). Amplification of 20336 genomic DNA with these two primers gave a mixed PCR product. One amplified PCR fragment was 1006 bp long (designated DCA1002). The DNA sequence for this fragment was determined and was found to have 85% identity to the DNA sequence for the *CYP52D4* gene of *C. tropicalis* 750. When this PCR product was used to screen the third genomic library one clone (pHKM12) was identified that contained a full-length *CYP52* gene along with 5' and 3' flanking sequences (Figure 9). The *CYP52* gene included regulatory and protein coding regions with an open reading frame of 1539 nucleotides long which encoded a putative CYP52 protein of 512 amino acids (Figures 15 and 16). This gene was designated as *CYP52A8A* (SEQ ID NO: 92) since its amino acid sequence (SEQ ID NO: 102) was most similar to the *CYP52A8* protein of *C. maltosa*. The protein coding region of the *CYP52A8A* gene is defined by nucleotides 464-2002 of SEQ ID NO: 92. The amino acid sequence of the *CYP52A8A* protein is set forth in SEQ ID NO: 102.

3) Cloning of *CYP52D4A*

The screening of the second genomic library with the HemeB1 (SEQ ID NO: 27) primer (Table 4) yielded a clone carrying a plasmid (pPA18) that contained a truncated gene having homology with the *CYP52D4* gene of *C. maltosa* (Figure 33). A 1.3 to 1.5-kb *Eco*RI-*Sst*I fragment from pPA18 containing part of the truncated *CYP* gene was isolated and used as a probe to screen the third genomic library for a full length *CYP52* gene. One clone (pHKM13) was isolated and found to contain a full-length *CYP* gene with extensive 5' and 3' flanking sequences (Figure 10). This gene has been designated as *CYP52D4A* (SEQ ID NO: 94) and the complete DNA including regulatory and protein coding regions (coding region defined by nucleotides 767-2266) and putative amino acid sequence (SEQ ID NO: 104) of this gene is shown in Figures 15 and 16. *CYP52D4A* (SEQ ID NO: 94) shares the greatest homology with the *CYP52D4* gene of *C. maltosa*.

4) **Cloning of *CYP52A2B* and *CYP52A8B***

A mixed probe containing *CYP52A1A, A2A, A3A, D4A, A5A* and *A8A* genes was used to screen the third genomic library and several putative positive clones were identified. Seven of these were sequenced with the degenerate primers Cyp52a (SEQ ID NO: 32), Cyp52b (SEQ ID NO: 33), Cyp52c (SEQ ID NO: 34) and Cyp52d (SEQ ID NO: 35) shown in Table 4. These primers were designed from highly conserved regions of the four *CYP52* subfamilies, namely *CYP52A, B, C & D*. Sequences from two clones, pHKM14 and pHKM15 (Figures 11 and 12), shared considerable homology with DNA sequence of the *C. tropicalis* 20336 *CYP52A2* and *CYP52A8* genes, respectively. The complete DNA (SEQ ID NO: 87) including regulatory and protein coding regions (coding region defined by nucleotides 1072-2640) and putative amino acid sequence (SEQ ID NO: 97) of the *CYP52* gene present in pHKM14 suggested that it is *CYP52A2B* (Figures 15 and 16). The complete DNA (SEQ ID NO: 93) including regulatory and protein coding regions (coding region defined by nucleotides 1017-2555) and putative amino acid sequence (SEQ ID NO: 103) of the *CYP52* gene present in pHKM15 suggested that it is *CYP52A8B* (Figures 15 and 16).

EXAMPLE 14

Identification of *CYP* and *CPR* Genes Induced by Selected Fatty Acid and Alkane Substrates

Genes whose transcription is turned on by the presence of selected fatty acid or alkane substrates have been identified using the QC-RT-PCR assay. This assay was used to measure (*CYP*) and (*CPR*) gene expression in fermentor grown cultures *C. tropicalis* ATCC 20962. This method involves the isolation of total cellular RNA from cultures of *C. tropicalis* and the quantification of a specific mRNA within that sample through the design and use of sequence specific QC-RT-PCR primers and an RNA competitor. Quantification is achieved through the use of known concentrations of highly homologous competitor RNA in the QC-RT-PCR reactions. The resulting QC-RT-PCR amplified cDNA's are separated and quantitated through the use of ion pairing reverse phase HPLC. This assay was used to characterize the expression of *CYP52* genes of *C. tropicalis* ATCC 20962 in response to various fatty acid and alkane substrates. Genes which were induced were identified by the calculation of their mRNA concentration at various times before and after induction. Figure 18 provides an example of

how the concentration of mRNA for *CYP52A5* can be calculated using the QC-RT-PCR assay. The log ratio of unknown (U) to competitor product (C) is plotted versus the concentration of competitor RNA present in the QC-RT-PCR reactions. The concentration of competitor which results in a log ratio of U/C of zero, represents the point where the unknown messenger RNA concentration is equal to the concentration of the competitor. Figure 18 allows for the calculation of the amount of *CYP52A5* message present in 100 ng of total RNA isolated from cell samples taken at 0, 1, and 2 hours after the addition of Emersol® 267 in a fermentor run. From this analysis, it is possible to determine the concentration of the *CYP52A5* mRNA present in 100 ng of total cellular RNA. In the plot contained in Figure 18 it takes 0.46 pg of competitor to equal the number of mRNA's of *CYP52A5* in 100 ng of RNA isolated from cells just prior (time 0) to the addition of the substrate, Emersol® 267. In cell samples taken at one and two hours after the addition of Emersol® 267 it takes 5.5 and 8.5 pg of competitor RNA, respectively. This result demonstrates that *CYP52A5* (SEQ ID NOS: 90 and 91) is induced more than 18 fold within two hours after the addition of Emersol® 267. This type of analysis was used to demonstrate that *CYP52A5* (SEQ ID NO: 90 and 91) is induced by Emersol® 267. Figure 19 shows the relative amounts of *CYP52A5* (SEQ ID NOS: 90 and 91) expression in fermentor runs with and without Emersol® 267 as a substrate. The differences in the *CYP52A5* (SEQ. ID NOS: 90 and 91) expression patterns are due to the addition of Emersol® 267 to the fermentation medium.

This analysis clearly demonstrates that expression of *CYP52A5* (SEQ ID NOS: 90 and 91) in *C. tropicalis* 20962 is inducible by the addition of Emersol® 267 to the growth medium. This analysis was performed to characterize the expression of *CYP52A2A* (SEQ ID NO: 86), *CYP52A3AB* (SEQ ID NOS: 88 and 89), *CYP52A8A* (SEQ ID NO: 92), *CYP52A1A* (SEQ ID NO: 85), *CYP52D4A* (SEQ ID NO: 94) and *CPRB* (SEQ ID NO: 82) in response to the presence of Emersol® 267 in the fermentation medium (Figure 20). The results of these analysis' indicate, that like the *CYP52A5* gene (SEQ ID NOS: 90 and 91) of *C. tropicalis* 20962, the *CYP52A2A* gene (SEQ ID NO: 86) is inducible by Emersol® 267. A small induction is observed for *CYP52A1A* (SEQ ID NO: 85) and *CYP52A8A* (SEQ ID NO: 92). In contrast, any induction for *CYP52D4A* (SEQ ID NO: 94), *CYP52A3A* (SEQ ID NO: 88), *CYP52A3B* (SEQ ID NO: 89) is below the level of detection of the assay. *CPRB* (SEQ ID NO: 82) is moderately induced by Emersol® 267, four to five fold. The results of these analysis are summarized in

Figure 20. Figure 34 provides an example of selective induction of *CYP52A* genes. When pure fatty acid or alkanes are spiked into a fermentor containing *C. tropicalis* 20962 or a derivative thereof, the transcriptional activation of *CYP52A* genes was detected using the QC-RT-PCR assay. Figure 34 shows that pure oleic acid (C18:1) strongly induces *CYP52A2A* (SEQ ID NO: 86) while inducing *CYP52A5* (SEQ ID NOS: 90 and 91). In the same fermentor addition of pure alkane (tridecane) shows strong induction of both *CYP52A2A* (SEQ ID NO: 86) and *CYP52A1A* (SEQ ID NO: 85). However, tridecane did not induce *CYP52A5* (SEQ ID NOS: 90 and 91). In a separate fermentation using ATCC 20962, containing pure octadecane as the substrate, induction of *CYP52A2A*, *CYP52A5A* and *CYP52A1A* is detected (see Figure 36). The foregoing demonstrates selective induction of particular *CYP* genes by specific substrates, thus providing techniques for selective metabolic engineering of cell strains. For example, if tridecane modification is desired, organisms engineered for high levels of *CYP52A2A* (SEQ ID NO: 86) and *CYP52A1A* (SEQ ID NO: 85) activity are indicated. If oleic acid modification is desired, organisms engineered for high levels of *CYP52A2A* (SEQ ID NO: 86) activity are indicated.

EXAMPLE 15

Integration of Selected *CYP* and *CPR* Genes into the Genome of *Candida tropicalis*

In order to integrate selected genes into the chromosome of *C. tropicalis* 20336 or its descendants, there has to be a target DNA sequence, which may or may not be an intact gene, into which the genes can be inserted. There must also be a method to select for the integration event. In some cases the target DNA sequence and the selectable marker are the same and, if so, then there must also be a method to regain use of the target gene as a selectable marker following the integration event. In *C. tropicalis* and its descendants, one gene which fits these criteria is *URA3A*, encoding orotidine-5'-phosphate decarboxylase. Using it as a target for integration, *ura*$^-$ variants of *C. tropicalis* can be transformed in such a way as to regenerate a *URA*$^+$ genotype via homologous recombination (Figure 21). Depending upon the design of the integration vector, one or more genes can be integrated into the genome at the same time. Using a split *URA3A* gene oriented as shown in Figure 22, homologous integration would yield at least one copy of the gene(s) of interest which are inserted between the split portions of the *URA3A* gene. Moreover, because of the high sequence similarity between *URA3A* and *URA3B* genes, integration of the

Figure 20. Figure 34 provides an example of selective induction of *CYP52A* genes. When pure fatty acid or alkanes are spiked into a fermentor containing *C. tropicalis* 20962 or a derivative thereof, the transcriptional activation of *CYP52A* genes was detected using the QC-RT-PCR assay. Figure 34 shows that pure oleic acid (C18:1) strongly induces *CYP52A2A* (SEQ ID NO: 86) while inducing *CYP52A5* (SEQ ID NOS: 90 and 91). In the same fermentor addition of pure alkane (tridecane) shows strong induction of both *CYP52A2A* (SEQ ID NO: 86) and *CYP52A1A* (SEQ ID NO: 85). However, tridecane did not induce *CYP52A5* (SEQ ID NOS: 90 and 91). In a separate fermentation using ATCC 20962, containing pure octadecane as the substrate, induction of *CYP52A2A*, *CYP52A5A* and *CYP52A1A* is detected (see Figure 36). The foregoing demonstrates selective induction of particular *CYP* genes by specific substrates, thus providing techniques for selective metabolic engineering of cell strains. For example, if tridecane modification is desired, organisms engineered for high levels of *CYP52A2A* (SEQ ID NO: 86) and *CYP52A1A* (SEQ ID NO: 85) activity are indicated. If oleic acid modification is desired, organisms engineered for high levels of *CYP52A2A* (SEQ ID NO: 86) activity are indicated.

EXAMPLE 15

Integration of Selected *CYP* and *CPR* Genes into the Genome of *Candida tropicalis*

In order to integrate selected genes into the chromosome of *C. tropicalis* 20336 or its descendants, there has to be a target DNA sequence, which may or may not be an intact gene, into which the genes can be inserted. There must also be a method to select for the integration event. In some cases the target DNA sequence and the selectable marker are the same and, if so, then there must also be a method to regain use of the target gene as a selectable marker following the integration event. In *C. tropicalis* and its descendants, one gene which fits these criteria is *URA3A*, encoding orotidine-5'-phosphate decarboxylase. Using it as a target for integration, *ura*$^-$ variants of *C. tropicalis* can be transformed in such a way as to regenerate a *URA*$^+$ genotype via homologous recombination (Figure 21). Depending upon the design of the integration vector, one or more genes can be integrated into the genome at the same time. Using a split *URA3A* gene oriented as shown in Figure 22, homologous integration would yield at least one copy of the gene(s) of interest which are inserted between the split portions of the *URA3A* gene. Moreover, because of the high sequence similarity between *URA3A* and *URA3B* genes, integration of the

construct can occur at both the *URA3A* and *URA3B* loci. Subsequently, an oligonucleotide designed with a deletion in a portion of the *URA* gene based on the identical sequence across both the *URA3A* and *URA3B* genes, can be utilized to yield *C. tropicalis* transformants which are once again *ura*⁻ but which still carry one or more newly integrated genes of choice (Figure 21). *ura*⁻ variants of *C. tropicalis* can also be isolated via other methods such as classical mutagenesis or by spontaneous mutation. Using well established protocols, selection of *ura*⁻ strains can be facilitated by the use of 5-fluoroorotic acid (5-FOA) as described, e.g., in Boeke et al., *Mol. Gen. Genet.* 197:345-346, (1984), incorporated herein by reference. The utility of this approach for the manipulation of *C. tropicalis* has been well documented as described, e.g., in Picataggio et al., *Mol. and Cell. Biol.* 11:4333-4339 (1991); Rohrer et al., *Appl. Microbiol. Biotechnol.* 36:650-654 (1992); Picataggio et al., *Bio/Technology* 10:894-898 (1992); U.S. Patent No. 5,648,247; U.S. Patent No. 5,620,878; U.S. Patent No. 5,204,252; U.S. Patent No. 5,254,466, all of which are incorporated herein by reference.

A. Construction of a URA Integration Vector, pURAin.

Primers were designed and synthesized based on the 1712 bp sequence of the *URA3A* gene of *C. tropicalis* 20336 (see Figure 23). The nucleotide sequence of the *URA3A* gene of *C. tropicalis* 20336 is set forth in SEQ ID NO: 105 and the amino acid sequence of the encoded protein is set forth in SEQ ID NO: 106. *URA3A* Primer Set #1a (SEQ ID NO: 9) and #1b (SEQ ID NO: 10) (Table 4) was used in PCR with *C. tropicalis* 20336 genomic DNA to amplify *URA3A* sequences between nucleotide 733 and 1688 as shown in Figure 23. The primers are designed to introduce unique 5' *Asc*I and 3' *Pac*I restriction sites into the resulting amplified *URA3A* fragment. *Asc*I and *Pac*I sites were chosen because these sites are not present within *CYP* or *CPR* genes identified to date. *URA3A* Primer Set #2 was used in PCR with *C. tropicalis* 20336 genomic DNA as a template, to amplify *URA3A* sequences between nucleotide 9 and 758 as shown in Figure 23. *URA3A* Primer set #2a (SEQ ID NO: 11) and #2b (SEQ ID NO: 12) (Table 4) was designed to introduce unique 5' *Pac*I and 3' *Pme*I restriction sites into the resulting amplified *URA3A* fragment. The *Pme*I site is also not present within *CYP* and *CPR* genes identified to date. PCR fragments of the *URA3A* gene were purified, restricted with *Asc*I, *Pac*I and *Pme*I restriction enzymes and ligated to a gel purified, QiaexII cleaned *Asc*I-*Pme*I digest of plasmid pNEB193 (Figure 25) purchased from New England Biolabs (Beverly, MA).

The ligation was performed with an equimolar number of DNA termini at 16 °C for 16 hr using T4 DNA ligase (New England Biolabs). Ligations were transformed into *E. coli* XL1-Blue cells (Stratagene, LaJolla, CA) according to manufacturers recommendations. White colonies were isolated, grown, plasmid DNA isolated and digested with *Asc*I-*Pme*I to confirm insertion of the modified *URA3A* into pNEB193. The resulting base integration vector was named pURAin (Figure 24).

B. Amplification of *CYP52A2A*, *CYP52A3A*, *CYP52A5A* and *CPRB* from *C. tropicalis* 20336 Genomic DNA

The genes encoding *CYP52A2A*, (SEQ ID NO: 86) and *CYP52A3A* (SEQ ID NO: 88) from *C. tropicalis* 20336 were amplified from genomic clones (pPA15 and pPA57, respectively) (Figures 26 and 29) via PCR using primers (Primer *CYP* 2A#1, SEQ ID NO: 1 and Primer *CYP* 2A#2, SEQ ID NO: 2 for CYP52A2A) (Primer *CYP* 3A#1, SEQ ID NO: 3 and Primer *CYP* 3A#2, SEQ ID NO: 4 for CYP52A3A) to introduce *Pac*I cloning sites. These PCR primers were designed based upon the DNA sequence determined for *CYP52A2A* (SEQ ID NO: 86) (Figure 15). The Ampli*Taq* Gold PCR kit (Perkin Elmer Cetus, Foster City, CA) was used according to manufacturers specifications. The *CYP52A2A* PCR amplification product was 2,230 base pairs in length , yielding 496 bp of DNA upstream of the *CYP52A2A* start codon and 168 bp downstream of the stop codon for the *CYP52A2A* ORF. The *CYP52A3A* PCR amplification product was 2154 base pairs in length, yielding 437bp of DNA upstream of the *CYP52A3A* start codon and 97bp downstream of the stop codon for the *CYP52A3A ORF*. The *CYP52A3A* PCR amplification product was 2154 base pairs in length, yielding 437bp of DNA upstream of the *CYP52A3A* start codon and 97bp downsteam of the stop codon for the *CYP52A3A* ORF.

The gene encoding *CYP52A5A* (SEQ ID NO: 90) from *C. tropicalis* 20336 was amplified from genomic DNA via PCR using primers (Primer *CYP* 5A#1, SEQ ID NO: 5 and Primer *CYP* 5A#2, SEQ ID NO: 6) to introduce *Pac*I cloning sites. These PCR primers were designed based upon the DNA sequence determined for *CYP52A5A* (SEQ ID NO: 90) . The Expand Hi-Fi *Taq* PCR kit (Boehringer Mannheim, Indianapolis, IN) was used according to manufacturers specifications. The *CYP52A5A* PCR amplification product was 3,298 base pairs in length.

The gene encoding *CPRB* (SEQ ID NO: 82) from *C. tropicalis* 20336 was amplified from genomic DNA via PCR using primers (*CPR* B#1, SEQ ID NO: 7 and *CPR* B#2, SEQ ID NO: 8) based upon the DNA sequence determined for *CPRB* (SEQ ID NO: 82) (Figure 13). These primers were designed to introduce unique *Pac*I cloning sites. The Expand Hi-Fi *Taq* PCR kit (Boehringer Mannheim, Indianapolis, IN) was used according to manufacturers specifications. The *CPRB* PCR product was 3266 bp in length, yielding 747 bp pf DNA upstream of the *CPRB* start codon and 493 bp downstream of the stop codon for the *CPRB* ORF. The resulting PCR products were isolated via agarose gel electrophoresis, purified using QiaexII and digested with *Pac*I. The PCR fragments were purified, desalted and concentrated using a Microcon 100 (Amicon, Beverly, MA).

The above described amplification procedures are applicable to the other genes listed in Table 5 using the respectively indicated primers.

C. Cloning of *CYP* and *CPR* Genes into pURAin.

The next step was to clone the selected *CYP* and *CPR* genes into the pURAin integration vector. In a preferred aspect of the present invention, no foreign DNA other than that specifically provided by synthetic restriction site sequences are incorporated into the DNA which was cloned into the genome of *C. tropicalis,* i.e., with the exception of restriction site DNA only native *C. tropicalis* DNA sequences are incorporated into the genome. pURAin was digested with *Pac*I, Qiaex II cleaned, and dephosphorylated with Shrimp Alkaline Phosphatase (SAP) (United States Biochemical, Cleveland, OH) according the manufacturer's recommendations. Approximately 500 ng of *Pac*I linearized pURAin was dephosphorylated for 1 hr at 37°C using SAP at a concentration of 0.2 Units of enzyme per 1 pmol of DNA termini. The reaction was stopped by heat inactivation at 65°C for 20 min.

The *CYP52A2A Pac*I fragment derived using the primer shown in Table 4 was ligated to plasmid pURAin which had also been digested with *Pac*I. *Pac*I digested pURAin was dephosphorylated, and ligated to the *CYP52A2A* ULTMA PCR product as described previously. The ligation mixture was transformed into *E. coli* XL1 Blue MRF' (Stratagene) and 2 resistant colonies were selected and screened for correct constructs which should contain vector sequence, the inverted *URA3A* gene, and the amplified *CYP52A2A* gene (SEQ ID NO: 86) of 20336. *AscI-PmeI* digestion identified one of the two constructs, plasmid pURA2in, as being correct (Figure

27). This plasmid was sequenced and compared to *CYP52A2A* (SEQ ID NO: 86) to confirm that PCR did not introduce DNA base changes that would result in an amino acid change.

Prior to its use, the *CPRB Pac*I fragment derived using the primers shown in Table 4 was sequenced and compared to *CPRB* (SEQ ID NO: 82) to confirm that PCR did not introduce DNA base pair changes that would result in an amino acid change. Following confirmation, *CPRB* (SEQ ID NO: 82) was ligated to plasmid pURAin which had also been digested with *Pac*I. *Pac*I digested pURAin was dephosphorylated, and ligated to the *CPR* Expand Hi-Fi PCR product as described previously. The ligation mixture was transformed into *E. coli* XL1 Blue MRF' (Stratagene) and several resistant colonies were selected and screened for correct constructs which should contain vector sequence, the inverted *URA3A* gene, and the amplified *CPRB* gene (SEQ ID NO: 82) of 20336. AscI-*Pme*I digestion confirmed a successful construct, pURAREDBin.

In a manner similar to the above, each of the other *CYP* and *CPR* genes disclosed herein are cloned into pURAin. *Pac*I fragments of these genes, whose sequences are given in Figures 13 and 15, are derivable by methods known to those skilled in the art.

1) Construction of Vectors Used to Generate HDC 20 and HDC 23

A previously constructed integration vector containing *CPRB* (SEQ ID NO: 82), pURAREDBin, was chosen as the starting vector. This vector was partially digested with *Pac*I and the linearized fragment was gel-isolated. The active *Pac*I was destroyed by treatment with T4 DNA polymerase and the vector was re-ligated. Subsequent isolation and complete digestion of this new plasmid yielded a vector now containing only one active *Pac*I site. This fragment was gel-isolated, dephosphorylated and ligated to the *CYP52A2A Pac*I fragment. Vectors that contain the *CYP52A2A* (SEQ ID NO: 86) and *CPRB* (SEQ ID NO: 82) genes oriented in the same direction, pURAin *CPR* 2A S, as well as opposite directions (5' ends connected), pURAin *CPR* 2A O, were generated.

D. Confirmation of *CYP* Integration (Figure 21 for Integration Scheme) into the Genome of *C. tropicalis*

Based on the construct, pURA2in, used to transform H5343 *ura*⁻, a scheme to detect integration was devised. Genomic DNA from transformants was digested with *Dra* III

and *Spe* I which are enzymes that cut within the *URA3A*, and *URA3B* genes but not within the integrated *CYP52A2A* gene. Digestion of genomic DNA where an integration had occurred at the *URA3A* or *URA3B* loci would be expected to result in a 3.5 kb or a 3.3 kb fragment, respectively (Figure 28). Moreover, digestion of the same genomic DNA with *Pac*I would yield a 2.2 kb fragment characteristic for the integrated *CYP52A2A* gene (Figure 28). Southern hybridizations of these digests with fragments of the *CYP52A2A* gene were used to screen for these integration events. Intensity of the band signal from the Southern using *Pac*I digestion was used as a measure of the number of integration events, ((i.e. the more copies of the *CYP52A2A* gene (SEQ ID NO: 86) which are present, the stronger the hybridization signal)).

C. tropicalis H5343 transformed *URA* prototrophs were grown at 30°C, 170 rpm, in 10 ml SC-uracil media for preparation of genomic DNA. Genomic DNA was isolated by the method described previously. Genomic DNA was digested with *Spe*I and *Dra*III. A 0.95% agarose gel was used to prepare a Southern hybridization blot. The DNA from the gel was transferred to a MagnaCharge nylon filter membrane (MSI Technologies, Westboro, MA) according to the alkaline transfer method of Sambrook et al., *supra*. For the Southern hybridization, a 2.2 kb *CYP52A2A* DNA fragment was used as a hybridization probe. 300 ng of *CYP52A2A* DNA was labeled using a ECL Direct labeling and detection system (Amersham) and the Southern was processed according to the ECL kit specifications. The blot was processed in a volume of 30 ml of hybridization fluid corresponding to 0.125 ml/cm^2. Following a prehybridization at 42°C for 1 hr, 300 ng of *CYP52A2A* probe was added and the hybridization continued for 16 hr at 42°C. Following hybridization, the blots were washed two times for 20 min each at 42 °C in primary wash containing urea. Two 5 min secondary washes at RT were conducted, followed by detection according to directions. The blots were exposed for 16 hours (hr) as recommended.

Integration was confirmed by the detection of a *Spe*I-*Dra*III 3.5 kb fragment from the genomic DNA of the transformants but not with the *C. tropicalis* 20336 control. Subsequently, a *Pac*I digestion of the genomic DNA of the positive transformants, followed by a Southern hybridization using an *CYP52A2A* gene probe, confirmed integration by the detection of a 2.2 kb fragment. The resulting *CYP52A2A* integrated strain was named HDC1 (see Table 1).

and *Spe* I which are enzymes that cut within the *URA3A*, and *URA3B* genes but not within the integrated *CYP52A2A* gene. Digestion of genomic DNA where an integration had occurred at the *URA3A* or *URA3B* loci would be expected to result in a 3.5 kb or a 3.3 kb fragment, respectively (Figure 28). Moreover, digestion of the same genomic DNA with *Pac*I would yield a 2.2 kb fragment characteristic for the integrated *CYP52A2A* gene (Figure 28). Southern hybridizations of these digests with fragments of the *CYP52A2A* gene were used to screen for these integration events. Intensity of the band signal from the Southern using *Pac*I digestion was used as a measure of the number of integration events, ((i.e. the more copies of the *CYP52A2A* gene (SEQ ID NO: 86) which are present, the stronger the hybridization signal)).

C. tropicalis H5343 transformed *URA* prototrophs were grown at 30°C, 170 rpm, in 10 ml SC-uracil media for preparation of genomic DNA. Genomic DNA was isolated by the method described previously. Genomic DNA was digested with *Spe*I and *Dra*III. A 0.95% agarose gel was used to prepare a Southern hybridization blot. The DNA from the gel was transferred to a MagnaCharge nylon filter membrane (MSI Technologies, Westboro, MA) according to the alkaline transfer method of Sambrook et al., *supra*. For the Southern hybridization, a 2.2 kb *CYP52A2A* DNA fragment was used as a hybridization probe. 300 ng of *CYP52A2A* DNA was labeled using a ECL Direct labeling and detection system (Amersham) and the Southern was processed according to the ECL kit specifications. The blot was processed in a volume of 30 ml of hybridization fluid corresponding to 0.125 ml/cm^2. Following a prehybridization at 42°C for 1 hr, 300 ng of *CYP52A2A* probe was added and the hybridization continued for 16 hr at 42°C. Following hybridization, the blots were washed two times for 20 min each at 42 °C in primary wash containing urea. Two 5 min secondary washes at RT were conducted, followed by detection according to directions. The blots were exposed for 16 hours (hr) as recommended.

Integration was confirmed by the detection of a *Spe*I-*Dra*III 3.5 kb fragment from the genomic DNA of the transformants but not with the *C. tropicalis* 20336 control. Subsequently, a *Pac*I digestion of the genomic DNA of the positive transformants, followed by a Southern hybridization using an *CYP52A2A* gene probe, confirmed integration by the detection of a 2.2 kb fragment. The resulting *CYP52A2A* integrated strain was named HDC1 (see Table 1).

In a manner similar to the above, each of the genes contained in the *Pac*I fragments which are described in Section 3c above were confirmed for integration into the genome of *C. tropicalis.*

Transformants generated by transformation with the vectors, pURAin *CPR* 2A S or pURAin *CPR* 2A O, were analyzed by Southern hybridization for integration of both the *CYP52A2A* (SEQ ID NO: 86) and *CPRB* (SEQ ID NO: 82) genes tandemly. Three strains were generated in which the *CYP52A2A* (SEQ ID NO: 86) and *CPRB* (SEQ ID NO: 82) genes integrated are in the opposite orientation (HDC 20-1, HDC 20-2 and HDC 20-3) and three were generated with the *CYP52A2A* (SEQ ID NO: 86) and *CPRB* (SEQ ID NO: 82) genes integrated in the same orientation (HDC 23-1, HDC 23-2 and HDC 23-3), Table 1.

E. Confirmation of *CPRB* Integration into H5343 *ura*

Seven transformants were screened by colony PCR using *CPRB* primer #2 (SEQ ID NO: 8) and a *URA3A*- specific primer. In five of the transformants, successful integration was detected by the presence of a 3899 bp PCR product. This 3899 bp PCR product represents the *CPRB* gene adjacent to the *URA3A* gene in the genome of H5343 thereby confirming integration. The resulting *CPRB* integrated strains were named HDC10-1 and HDC10-2 (see Table 1).

F. Strain Evaluation.

As determined by quantitative PCR, when compared to parent H5343, HDC10-1 contained three additional copies of the reductase gene and HDC10-2 contained four additional copies of the reductase gene. Evaluations of HDC20-1, HDC20-2 and HDC20-3 based on Southern hybridization data indicates that HDC20-1 contained multiple integrations, i.e., 2 to 3 times that of HDC20-2 or HDC20-3. Evaluations of HDC23-1, HDC23-2, and HDC23-3 based on Southern hybridization data indicates that HDC23-3 contained multiple integrations, i.e., 2 to 3 times that of HDC23-1 or HDC23-2. The data in Table 8 indicates that the integration of components of the ω-hydroxylase complex have a positive effect on the improvement of *Candida tropicalis* ATCC 20962 as a biocatalyst. The results indicate that *CYP52A5A* (SEQ ID NO: 90) is an important gene for the conversion of oleic acid to diacid. Surprisingly, tandem integrations of *CYP* and *CPR* genes oriented in the opposite direction (HDC 20 strains) seem to

be less productive than tandem integrations oriented in the same direction (HDC 23 strains), Tables 1 and 8.

CHART

Media Composition

LB Broth

Bacto Tryptone	10 g
Bacto Yeast Extract	5 g
Sodium Chloride	10 g
Distilled Water	1,000 ml

LB Agar

Bacto Tryptone	10 g
Bacto Yeast Extract	5 g
Sodium Chloride	10 g
Agar	15 g
Distilled Water	1,000 ml

LB Top Agarose

Bacto Tryptone	10 g
Bacto Yeast Extract	5 g
Sodium Chloride	10 g
Agarose	7 g
Distilled Water	1,000 ml

NZCYM Broth

Bacto Casein Digest	10 g
Bacto Casamino Acids	1 g
Bacto Yeast Extract	5 g
Sodium Chloride	5 g
Magnesium Sulfate (anhydrous)	0.98 g
Distilled Water	1,000 ml

NZCYM Agar

Bacto Casein Digest	10 g
Bacto Casamino Acids	1 g
Bacto Yeast Extract	5 g
Sodium Chloride	5 g
Magnesium Sulfate (anhydrous)	0.98 g
Agar	15 g
Distilled Water	1,000 ml

NZCYM Top Agarose

Bacto Casein Digest	10 g
Bacto Casamino Acids	1 g
Bacto Yeast Extract	5 g
Sodium Chloride	5 g
Magnesium Sulfate (anhydrous)	0.98 g
Agarose	7 g
Distilled Water	1,000 ml

YEPD Broth

Bacto Yeast Extract	10 g
Bacto Peptone	20 g
Glucose	20 g
Distilled Water	1,000 ml

YEPD Agar*

Bacto Yeast Extract	10 g
Bacto Peptone	20 g
Glucose	20 g
Agar	20 g
Distilled Water	1,000 ml

SC - uracil*

Bacto-yeast nitrogen base without amino acids	6.7g
Glucose	20g
Bacto-agar	20g
Drop-out mix	2g
Distilled water	1,000ml

DCA2 medium	g/l
Peptone	3.0
Yeast Extract	6.0
Sodium Acetate	3.0
Yeast Nitrogen Base (Difco)	6.7
Glucose (anhydrous)	50.0
Potassium Phosphate (dibasic, trihydrate)	7.2
Potassium Phosphate (monobasic, anhydrous)	9.3

DCA3 medium	g/l
0.3 M Phosphate buffer containing, pH 7.5	
Glycerol	50
Yeast Nitrogen base (Difco)	6.7

Drop-out mix

Adenine	0.5g	Alanine	2g
Arginine	2g	Asparagine	2g
Aspartic acid	2g	Cysteine	2g
Glutamine	2g	Glutamic acid	2g
Glycine	2g	Histidine	2g
Inositol	2g	Isoleucine	2g
Leucine	10g	Lysine	2g
Methionine	2g	para-Aminobenzoic acid	0.2g
Phenylalanine	2g	Proline	2g
Serine	2g	Threonine	2g
Tryptophan	2g	Tyrosine	2g
Valine	2g		

*See Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Laboratory Press, USA (1994), incorporated herein by reference.

It will be understood that various modifications may be made to the embodiments and/or examples disclosed herein. Thus, the above description should not be construed as limiting, but merely as exemplifications of preferred embodiments. Those skilled in the art will envision other modifications within the scope and spirit of the claims appended hereto.

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WHAT IS CLAIMED IS:

1. Isolated nucleic acid encoding a *CPRA* protein having the amino acid sequence set forth in SEQ ID NO: 83.

2. Isolated nucleic acid comprising a coding region defined by nucleotides 1006-3042 as set forth in SEQ ID NO: 81.

3. Isolated nucleic acid according to claim 2 comprising the nucleotide sequence as set forth in SEQ ID NO: 81.

4. Isolated protein comprising an amino acid sequence as set forth in SEQ ID NO: 83.

5. A vector comprising a nucleotide sequence encoding *CPRA* protein including an amino acid sequence as set forth in SEQ ID NO: 83.

6. A vector according to claim 5 wherein the nucleotide sequence is set forth in nucleotides 1006-3042 of SEQ ID NO: 81

7. A vector according to claim 5 wherein the vector is selected from the group consisting of plasmid, phagemid, phage and cosmid.

8. A host cell transfected or transformed with the nucleic acid of claim 1.

9. A host cell according to claim 8 wherein the host cell is a yeast cell.

10. A host cell according to claim 9 wherein the yeast cell is a *Candida sp.*

11. A host cell according to claim 10 wherein the *Candida sp.* is *Candida tropicalis.*

12. A host cell according to claim 11 wherein the *Candida tropicalis* is *Candida tropicalis* 20336.

13. A host cell according to claim 12 wherein the *Candida tropicalis* is H5343 ura-.

14. A method of producing a *CPRA* protein including an amino acid sequence as set forth in SEQ ID NO: 83 comprising:

a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 83; and

b) culturing the cell under conditions favoring the expression of the protein.

15. The method according to claim 14 wherein the step of culturing the cell comprises adding an organic substrate to media containing the cell.

16. Isolated nucleic acid encoding a *CPRB* protein having the amino acid sequence set forth in SEQ ID NO: 84.

17. Isolated nucleic acid comprising a coding region defined by nucleotides 1033-3069 as set forth in SEQ ID NO: 82.

18. Isolated nucleic acid according to claim 17 comprising the nucleotide sequence as set forth in SEQ ID NO: 82.

19. Isolated protein comprising an amino acid sequence as set forth in SEQ ID NO: 84.

20. A vector comprising a nucleotide sequence encoding *CPRB* protein including an amino acid sequence as set forth in SEQ ID NO: 84.

21. A vector according to claim 20 wherein the nucleotide sequence is set forth in nucleotides 1033-3069 of SEQ ID NO: 82.

22. A vector according to claim 20 wherein the vector is selected from the group consisting of plasmid, phagemid, phage and cosmid..

23. A host cell transfected or transformed with the nucleic acid of claim 16.

24. A host cell according to claim 23 wherein the host cell is a yeast cell.

25. A host cell according to claim 24 wherein the yeast cell is a *Candida sp.*

26. A host cell according to claim 25 wherein the *Candida sp.* is *Candida tropicalis.*

27. A host cell according to claim 26 wherein the *Candida tropicalis* is *Candida tropicalis* 20336.

28. A host cell according to claim 27 wherein the *Candida tropicalis* is H5343 ura-.

29. A method of producing a *CPRB* protein including an amino acid sequence as set forth in SEQ ID NO: 84 comprising:

a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 84; and

b) culturing the cell under conditions favoring the expression of the protein.

30. The method according to claim 29 wherein the step of culturing the cell comprises adding an organic substrate to media containing the cell.

31. Isolated nucleic acid encoding a *CYP52A1A* protein having the amino acid sequence set forth in SEQ ID NO: 95.

32. Isolated nucleic acid comprising a coding region defined by nucleotides 1177-2748 as set forth in SEQ ID NO: 85.

33. Isolated nucleic acid according to claim 32 comprising the nucleotide sequence as set forth in SEQ ID NO: 85.

34. Isolated protein comprising an amino acid sequence as set forth in SEQ ID NO: 95.

35. A vector comprising a nucleotide sequence encoding *CYP52A1A* protein including an amino acid sequence as set forth in SEQ ID NO: 95.

36. A vector according to claim 35 wherein the nucleotide sequence is set forth in nucleotides 1177-2748 of SEQ ID NO: 85.

37. A vector according to claim 35 wherein the vector is selected from the group consisting of plasmid, phagemid, phage and cosmid.

38. A host cell transfected or transformed with the nucleic acid of claim 31.

39. A host cell according to claim 38 wherein the host cell is a yeast cell.

40. A host cell according to claim 39 wherein the yeast cell is a *Candida sp.*

41. A host cell according to claim 40 wherein the *Candida sp.* is *Candida tropicalis.*

42. A host cell according to claim 41 wherein the *Candida tropicalis* is *Candida tropicalis* 20336.

43. A host cell according to claim 42 wherein the *Candida tropicalis* is H5343 ura-.

44. A method of producing a *CYP52A1A* protein including an amino acid sequence as set forth in SEQ ID NO: 95 comprising:

a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 95; and

b) culturing the cell under conditions favoring the expression of the protein.

45. The method according to claim 44 wherein the step of culturing the cell comprises adding an organic substrate to media containing the cell.

46. Isolated nucleic acid encoding a *CYP52A2A* protein having the amino acid sequence set forth in SEQ ID NO: 96.

47. Isolated nucleic acid comprising a coding region defined by nucleotides 1199-2767 as set forth in SEQ ID NO: 86.

48. Isolated nucleic acid according to claim 47 comprising the nucleotide sequence as set forth in SEQ ID NO: 86.

49. Isolated protein comprising an amino acid sequence as set forth in SEQ ID NO: 96.

50. A vector comprising a nucleotide sequence encoding *CYP52A2A* protein including an amino acid sequence as set forth in SEQ ID NO: 96.

51. A vector according to claim 50 wherein the nucleotide sequence is set forth in nucleotides 1199-2767 of SEQ ID NO: 86.

52. A vector according to claim 50 wherein the vector is selected from the group consisting of plasmid, phagemid, phage and cosmid.

53. A host cell transfected or transformed with the nucleic acid of claim 46.

54. A host cell according to claim 53 wherein the host cell is a yeast cell.

55. A host cell according to claim 54 wherein the yeast cell is a *Candida sp.*

56. A host cell according to claim 55 wherein the *Candida sp.* is *Candida tropicalis.*

57. A host cell according to claim 56 wherein the *Candida tropicalis* is *Candida tropicalis* 20336.

58. A host cell according to claim 57 wherein the *Candida tropicalis* is H5343 ura-.

59. A method of producing a *CYP52A2A* protein including an amino acid sequence as set forth in SEQ ID NO: 96 comprising:

a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 96; and

b) culturing the cell under conditions favoring the expression of the protein.

60. The method according to claim 59 wherein the step of culturing the cell comprises adding an organic substrate to media containing the cell.

61. Isolated nucleic acid encoding a *CYP52A2B* protein having the amino acid sequence set forth in SEQ ID NO: 97.

62. Isolated nucleic acid comprising a coding region defined by nucleotides 1072-2640 as set forth in SEQ ID NO: 87.

63. Isolated nucleic acid according to claim 62 comprising the nucleotide sequence as set forth in SEQ ID NO: 87.

64. Isolated protein comprising an amino acid sequence as set forth in SEQ ID NO: 97.

65. A vector comprising a nucleotide sequence encoding *CYP52A2B* protein including an amino acid sequence as set forth in SEQ ID NO: 97.

66. A vector according to claim 65 wherein the nucleotide sequence is set forth in nucleotides 1072-2640 of SEQ ID NO: 87.

67. A vector according to claim 65 wherein the vector is selected from the group consisting of plasmid, phagemid, phage and cosmid.

68. A host cell transfected or transformed with the nucleic acid of claim 61.

69. A host cell according to claim 68 wherein the host cell is a yeast cell.

70. A host cell according to claim 69 wherein the yeast cell is a *Candida sp.*

71. A host cell according to claim 70 wherein the *Candida sp.* is *Candida tropicalis.*

72. A host cell according to claim 71 wherein the *Candida tropicalis* is *Candida tropicalis* 20336.

73. A host cell according to claim 72 wherein the *Candida tropicalis* is H5343 ura-.

74. A method of producing a *CYP52A2B* protein including an amino acid sequence as set forth in SEQ ID NO: 97 comprising:

a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 97; and

b) culturing the cell under conditions favoring the expression of the protein.

75. The method according to claim 74 wherein the step of culturing the cell comprises adding an organic substrate to media containing the cell.

76. Isolated nucleic acid encoding a *CYP52A3A* protein having the amino acid sequence set forth in SEQ ID NO: 98.

77. Isolated nucleic acid comprising a coding region defined by nucleotides 1126-2748 as set forth in SEQ ID NO: 88.

78. Isolated nucleic acid according to claim 77 comprising the nucleotide sequence as set forth in SEQ ID NO: 88.

79. Isolated protein comprising an amino acid sequence as set forth in SEQ ID NO: 98.

80. A vector comprising a nucleotide sequence encoding *CYP52A3A* protein including an amino acid sequence as set forth in SEQ ID NO: 98.

81. A vector according to claim 80 wherein the nucleotide sequence is set forth in nucleotides 1126-2748 of SEQ ID NO: 88.

82. A vector according to claim 80 wherein the vector is selected from the group consisting of plasmid, phagemid, phage and cosmid.

83. A host cell transfected or transformed with the nucleic acid of claim 76.

84. A host cell according to claim 83 wherein the host cell is a yeast cell.

85. A host cell according to claim 84 wherein the yeast cell is a *Candida sp.*

86. A host cell according to claim 85 wherein the *Candida sp.* is *Candida tropicalis.*

87. A host cell according to claim 86 wherein the *Candida tropicalis* is *Candida tropicalis* 20336.

88. A host cell according to claim 87 wherein the *Candida tropicalis* is H5343 ura-.

89. A method of producing a *CYP52A3A* protein including an amino acid sequence as set forth in SEQ ID NO: 98 comprising:

a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 98; and

b) culturing the cell under conditions favoring the expression of the protein.

90. The method according to claim 89 wherein the step of culturing the cell comprises adding an organic substrate to media containing the cell.

91. Isolated nucleic acid encoding a *CYP52A3B* protein having the amino acid sequence as set forth in SEQ ID NO: 99.

92. Isolated nucleic acid comprising a coding region defined by nucleotides 913-2535 as set forth in SEQ ID NO: 89.

93. Isolated nucleic acid according to claim 92 comprising the nucleotide sequence as set forth in SEQ ID NO: 89.

94. Isolated protein comprising an amino acid sequence as set forth in SEQ ID NO: 99.

95. A vector comprising a nucleotide sequence encoding *CYP52A3B* protein including an amino acid sequence as set forth in SEQ ID NO: 99.

96. A vector according to claim 95 wherein the nucleotide sequence is set forth in nucleotides 913-2535 of SEQ ID NO: 89.

97. A vector according to claim 95 wherein the vector is selected from the group consisting of plasmid, phagemid, phage and cosmid.

98. A host cell transfected or transformed with the nucleic acid of claim 91.

99. A host cell according to claim 98 wherein the host cell is a yeast cell.

100. A host cell according to claim 99 wherein the yeast cell is a *Candida sp.*

101. A host cell according to claim 100 wherein the *Candida sp.* is *Candida tropicalis.*

102. A host cell according to claim 101 wherein the *Candida tropicalis* is *Candida tropicalis* 20336.

103. A host cell according to claim 102 wherein the *Candida tropicalis* is H5343 ura-.

104. A method of producing a *CYP52A3B* protein including an amino acid sequence as set forth in SEQ ID NO: 99 comprising:

a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 99; and

b) culturing the cell under conditions favoring the expression of the protein.

105. The method according to claim 104 wherein the step of culturing the cell comprises adding an organic substrate to media containing the cell.

106. Isolated nucleic acid encoding a *CYP52A5A* protein having the amino acid sequence set forth in SEQ ID NO: 100.

107. Isolated nucleic acid comprising a coding region defined by nucleotides 1103-2656 as set forth in SEQ ID NO: 90.

108. Isolated nucleic acid according to claim 107 comprising the nucleotide sequence as set forth in SEQ ID NO: 90.

109. Isolated protein comprising an amino acid sequence as set forth in SEQ ID NO: 100.

110. A vector comprising a nucleotide sequence encoding *CYP52A5A* protein including an amino acid sequence as set forth in SEQ ID NO: 100.

111. A vector according to claim 110 wherein the nucleotide sequence is set forth in nucleotides 1103-2656 OF SEQ ID NO: 90.

112. A vector according to claim 110 wherein the vector is selected from the group consisting of plasmid, phagemid, phage and cosmid.

113. A host cell transfected or transformed with the nucleic acid of claim 106.

114. A host cell according to claim 113 wherein the host cell is a yeast cell.

115. A host cell according to claim 114 wherein the yeast cell is a *Candida sp.*

116. A host cell according to claim 115 wherein the *Candida sp.* is *Candida tropicalis.*

117. A host cell according to claim 116 wherein the *Candida tropicalis* is *Candida tropicalis* 20336.

118. A host cell according to claim 117 wherein the *Candida tropicalis* is H5343 ura-.

119. A method of producing a *CYP52A5A* protein including an amino acid sequence as set forth in SEQ ID NO: 100 comprising:

a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 100; and

b) culturing the cell under conditions favoring the expression of the protein.

120. The method according to claim 119 wherein the step of culturing the cell comprises adding an organic substrate to media containing the cell.

121. Isolated nucleic acid encoding a *CYP52A5B* protein having the amino acid sequence as set forth in SEQ ID NO: 101.

122. Isolated nucleic acid comprising a coding region defined by nucleotides 1142-2695 as set forth in SEQ ID NO: 91.

123. Isolated nucleic acid according to claim 122 comprising the nucleotide sequence as set forth in SEQ ID NO: 91.

124. Isolated protein comprising an amino acid sequence as set forth in SEQ ID NO: 101.

125. A vector comprising a nucleotide sequence encoding *CYP52A5B* protein including the amino acid sequence as set forth in SEQ ID NO: 101.

126. A vector according to claim 125 wherein the nucleotide sequence is set forth in nucleotides 1142-2695 of SEQ ID NO: 91.

127. A vector according to claim 125 wherein the vector is selected from the group consisting of plasmid, phagemid, phage and cosmid.

128. A host cell transfected or transformed with the nucleic acid of claim 121.

129. A host cell according to claim 128 wherein the host cell is a yeast cell.

130. A host cell according to claim 129 wherein the yeast cell is a *Candida sp.*

131. A host cell according to claim 130 wherein the *Candida sp.* is *Candida tropicalis.*

132. A host cell according to claim 131 wherein the *Candida tropicalis* is *Candida tropicalis* 20336.

133. A host cell according to claim 132 wherein the *Candida tropicalis* is H5343 ura-.

134. A method of producing a *CYP52A5B* protein including an amino acid sequence as set forth in SEQ ID NO: 101 comprising:

a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 101; and

b) culturing the cell under conditions favoring the expression of the protein.

135. The method according to claim 134 wherein the step of culturing the cell comprises adding an organic substrate to media containing the cell.

136. Isolated nucleic acid encoding a *CYP52A8A* protein having the amino acid sequence set forth in SEQ ID NO: 102.

137. Isolated nucleic acid comprising a coding region defined by nucleotides 464-2002 as set forth in SEQ ID NO: 92.

138. Isolated nucleic acid according to claim 137 comprising the nucleotide sequence as set forth in SEQ ID NO: 92.

139. Isolated protein comprising an amino acid sequence as set forth in SEQ ID NO: 102.

140. A vector comprising a nucleotide sequence encoding *CYP52A8A* protein including an amino acid sequence as set forth in SEQ ID NO: 102.

141. A vector according to claim 140 wherein the nucleotide sequence is set forth in nucleotides 464-2002 of SEQ ID NO: 92.

142. A vector according to claim 140 wherein the vector is selected from the group consisting of plasmid, phagemid, phage and cosmid.

143. A host cell transfected or transformed with the nucleic acid of claim 136.

144. A host cell according to claim 143 wherein the host cell is a yeast cell.

145. A host cell according to claim 144 wherein the yeast cell is a *Candida sp.*

146. A host cell according to claim 145 wherein the *Candida sp.* is *Candida tropicalis.*

147. A host cell according to claim 146 wherein the *Candida tropicalis* is *Candida tropicalis* 20336.

148. A host cell according to claim 147 wherein the *Candida tropicalis* is H5343 ura-.

149. A method of producing a *CYP52A8A* protein including an amino acid sequence as set forth in SEQ ID NO: 102 comprising:

a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 102; and

b) culturing the cell under conditions favoring the expression of the protein.

150. The method according to claim 149 wherein the step of culturing the cell comprises adding an organic substrate to media containing the cell.

151. Isolated nucleic acid encoding a *CYP52A8B* protein having the amino acid sequence set forth in SEQ ID NO: 103.

152. Isolated nucleic acid comprising a coding region defined by nucleotides 1017-2555 as set forth in SEQ ID NO: 93.

153. Isolated nucleic acid according to claim 152 comprising the nucleotide sequence as set forth in SEQ ID NO: 93.

154. Isolated protein comprising an amino acid sequence as set forth in SEQ ID NO: 103.

155. A vector comprising a nucleotide sequence encoding *CYP52A8B* protein including an amino acid sequence as set forth in SEQ ID NO: 103.

156. A vector according to claim 155 wherein the nucleotide sequence is set forth in nucleotides 1017-2555 of SEQ ID NO: 93.

157. A vector according to claim 155 wherein the vector is selected from the group consisting of plasmid, phagemid, phage and cosmid.

158. A host cell transfected or transformed with the nucleic acid of claim 151.

159. A host cell according to claim 158 wherein the host cell is a yeast cell.

160. A host cell according to claim 159 wherein the yeast cell is a *Candida sp.*

161. A host cell according to claim 160 wherein the *Candida sp.* is *Candida tropicalis.*

162. A host cell according to claim 161 wherein the *Candida tropicalis* is *Candida tropicalis* 20336.

163. A host cell according to claim 162 wherein the *Candida tropicalis* is H5343 ura-.

164. A method of producing a *CYP52A8B* protein including an amino acid sequence as set forth in SEQ ID NO: 103 comprising:

a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 103; and

b) culturing the cell under conditions favoring the expression of the protein.

165. The method according to claim 164 wherein the step of culturing the cell comprises adding an organic substrate to media containing the cell.

166. Isolated nucleic acid encoding a *CYP52D4A* protein having the amino acid sequence set forth in SEQ ID NO: 104.

167. Isolated nucleic acid comprising a coding region defined by nucleotides 767-2266 as set forth in SEQ ID NO: 94.

168. Isolated nucleic acid according to claim 167 comprising the nucleotide sequence as set forth in SEQ ID NO: 94.

169. Isolated protein comprising an amino acid sequence as set forth in SEQ ID NO: 104.

170. A vector comprising a nucleotide sequence encoding *CYP52D4A* protein including an amino acid sequence as set forth in SEQ ID NO: 104.

171. A vector according to claim 170 wherein the nucleotide sequence is set forth in nucleotides 767-2266 of SEQ ID NO: 94.

172. A vector according to claim 170 wherein the vector is selected from the group consisting of plasmid, phagemid, phage and cosmid.

173. A host cell transfected or transformed with the nucleic acid of claim 166.

174. A host cell according to claim 173 wherein the host cell is a yeast cell.

175. A host cell according to claim 174 wherein the yeast cell is a *Candida sp.*

176. A host cell according to claim 175 wherein the *Candida sp.* is *Candida tropicalis.*

177. A host cell according to claim 176 wherein the *Candida tropicalis* is *Candida tropicalis* 20336.

178. A host cell according to claim 177 wherein the *Candida tropicalis* is H5343 ura-.

179. A method of producing a *CYP52D4A* protein including an amino acid sequence as set forth in SEQ ID NO: 104 comprising:

a) transforming a suitable host cell with a DNA sequence that encodes the protein having the amino acid sequence as set forth in SEQ ID NO: 104; and

b) culturing the cell under conditions favoring the expression of the protein.

180. The method according to claim 179 wherein the step of culturing the cell comprises adding an organic substrate to media containing the cell.

181. A method for discriminating members of a gene family by quantifying the amount of target mRNA in a sample comprising:

a) providing an organism containing a target gene;

b) culturing the organism with an organic substrate which causes upregulation in the activity of the target gene;

c) obtaining a sample of total RNA from the organism at a first point in time;

d) combining at least a portion of the sample of the total RNA with a known amount of competitor RNA to form an RNA mixture, wherein the competitor RNA is substantially similar to the target mRNA but has a lesser number of nucleotides compared to the target mRNA;

e) adding reverse transcriptase to the RNA mixture in a quantity sufficient to form corresponding target DNA and competitor DNA;

f) conducting a polymerase chain reaction in the presence of at least one primer specific for at least one substantially non-homologous region of the target DNA within the gene family, the primer also specific for the competitor DNA;

g) repeating steps (c-f) using increasing amounts of the competitor RNA while maintaining a substantially constant amount of target RNA;

(h) determining the point at which the amount of target DNA is substantially equal to the amount of competitor DNA;

(i) quantifying the results by comparing the ratio of the concentration of unknown target to the known concentration of competitor; and

(j) obtaining a sample of total RNA from the organism at another point in time and repeating steps (d-i).

182. A method according to claim 181 wherein the target gene is selected from the group consisting of a *CPR* gene and a *CYP* gene.

183. A method according to claim 182 wherein the *CPR* gene is selected from the group consisting of a *CPRA* gene (SEQ ID NO: 81) and a *CPRB* gene (SEQ ID NO: 82).

184. A method according to claim 182 wherein the *CYP* gene is selected from the group consisting of *CYP52A1A* gene (SEQ ID NO: 85), *CYP52A2A* gene (SEQ ID NO: 86), *CYP52A2B* gene (SEQ ID NO: 87), *CYP52A3A* gene (SEQ ID NO: 88), *CYP52A3B* gene (SEQ ID NO. 89), *CYP52A5A* gene (SEQ ID NO: 90), *CYP52A5B* gene (SEQ ID NO: 91), *CYP52A8A* gene (SEQ ID NO: 92), *CYP52A8B* gene (SEQ ID NO: 93) and *CYP52D4A* gene (SEQ ID NO: 94).

185. A method for increasing production of a dicarboxylic acid comprising:

a) providing a host cell having a naturally occurring number of *CPRA* genes;

b) increasing, in the host cell, the number of *CPRA* genes which encode a *CPRA* protein having the amino acid sequence as set forth in SEQ ID NO: 83;

c) culturing the host cell in media containing an organic substrate which upregulates the *CPRA* gene, to effect increased production of dicarboxylic acid.

186. A method for increasing the production of a *CPRA* protein having an amino acid sequence as set forth in SEQ ID NO: 83 comprising:

a) transforming a host cell having a naturally occurring amount of *CPRA* protein with an increased copy number of a *CPRA* gene that encodes the *CPRA* protein having the amino acid sequence as set forth in SEQ ID NO: 83; and

b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CPRA* gene.

187. A method for increasing production of a dicarboxylic acid comprising:

a) providing a host cell having a naturally occurring number of *CPRB* genes;

b) increasing, in the host cell, the number of *CPRB* genes which encode a *CPRB* protein having the amino acid sequence as set forth in SEQ ID NO: 84;

c) culturing the host cell in media containing an organic substrate which upregulates the *CPRB* gene, to effect increased production of dicarboxylic acid.

188. A method for increasing the production of a *CPRB* protein having an amino acid sequence as set forth in SEQ ID NO: 84 comprising:

a) transforming a host cell having a naturally occurring amount of *CPRB* protein with an increased copy number of a *CPRB* gene that encodes the *CPRB* protein having the amino acid sequence as set forth in SEQ ID NO: 84; and

b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CPRB* gene.

189. A method for increasing production of a dicarboxylic acid comprising:

a) providing a host cell having a naturally occurring number of *CYP52A1A* genes;

b) increasing, in the host cell, the number of *CYP52A1A* genes which encode a *CYP52A1A* protein having the amino acid sequence as set forth in SEQ ID NO: 95;

c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A2A* gene, to effect increased production of dicarboxylic acid.

190. A method for increasing the production of a *CYP52A1A* protein having an amino acid sequence as set forth in SEQ ID NO: 95 comprising:

a) transforming a host cell having a naturally occurring amount of *CYP52A1A* protein with an increased copy number of a *CYP52A1A* gene that encodes the *CYP52A1A* protein having the amino acid sequence as set forth in SEQ ID NO: 95; and

b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A1A* gene.

191. A method for increasing production of a dicarboxylic acid comprising:

a) providing a host cell having a naturally occurring number of *CYP52A2A* genes;

b) increasing, in the host cell, the number of *CYP52A2A* genes which encode a *CYP52A2A* protein having the amino acid sequence as set forth in SEQ ID NO: 96;

c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A2A* gene, to effect increased production of dicarboxylic acid.

192. A method for increasing the production of a *CYP52A2A* protein having an amino acid sequence as set forth in SEQ ID NO: 96 comprising:

a) transforming a host cell having a naturally occurring amount of *CYP52A2A* protein with an increased copy number of a *CYP52A2A* gene that encodes the *CYP52A2A* protein having the amino acid sequence as set forth in SEQ ID NO: 96; and

b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A2A* gene.

193. A method for increasing production of a dicarboxylic acid comprising:

a) providing a host cell having a naturally occurring number of *CYP52A2B* genes;

b) increasing, in the host cell, the number of *CYP52A2B* genes which encode a *CYP52A2B* protein having the amino acid sequence as set forth in SEQ ID NO: 97;

c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A2B* gene, to effect increased production of dicarboxylic acid.

194. A method for increasing the production of a *CYP52A2B* protein having an amino acid sequence as set forth in SEQ ID NO: 97 comprising:

a) transforming a host cell having a naturally occurring amount of *CYP52A2B* protein with an increased copy number of a *CYP52A2B* gene that encodes the *CYP52A2B* protein having the amino acid sequence as set forth in SEQ ID NO: 97; and

b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A2B* gene.

195. A method for increasing production of a dicarboxylic acid comprising:

a) providing a host cell having a naturally occurring number of *CYP52A3A* genes;

b) increasing, in the host cell, the number of *CYP52A3A* genes which encode a *CYP52A3A* protein having the amino acid sequence as set forth in SEQ ID NO: 98;

c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A3A* gene, to effect increased production of dicarboxylic acid.

196. A method for increasing the production of a *CYP52A3A* protein having an amino acid sequence as set forth in SEQ ID NO: 98 comprising:

a) transforming a host cell having a naturally occurring amount of *CYP52A3A* protein with an increased copy number of a *CYP52A3A* gene that encodes the *CYP52A3A* protein having the amino acid sequence as set forth in SEQ ID NO: 98; and

b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A3A* gene.

197. A method for increasing production of a dicarboxylic acid comprising:

a) providing a host cell having a naturally occurring number of *CYP52A3B* genes;

b) increasing, in the host cell, the number of *CYP52A3B* genes which encode a *CYP52A3B* protein having the amino acid sequence as set forth in SEQ ID NO: 99;

c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A3B* gene, to effect increased production of dicarboxylic acid.

198. A method for increasing the production of a *CYP52A3B* protein having an amino acid sequence as set forth in SEQ ID NO: 99 comprising:

a) transforming a host cell having a naturally occurring amount of *CYP52A3B* protein with an increased copy number of a *CYP52A3B* gene that encodes the *CYP52A3B* protein having the amino acid sequence as set forth in SEQ ID NO: 99; and

b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A3B* gene.

199. A method for increasing production of a dicarboxylic acid comprising:

a) providing a host cell having a naturally occurring number of *CYP52A5A* genes;

b) increasing, in the host cell, the number of *CYP52A5A* genes which encode a *CYP52A5A* protein having the amino acid sequence as set forth in SEQ ID NO: 100;

c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A5A* gene, to effect increased production of dicarboxylic acid.

200. A method for increasing the production of a *CYP52A5A* protein having an amino acid sequence as set forth in SEQ ID NO: 100 comprising:

a) transforming a host cell having a naturally occurring amount of *CYP52A5A* protein with an increased copy number of a *CYP52A5A* gene that encodes the *CYP52A5A* protein having the amino acid sequence as set forth in SEQ ID NO: 100; and

b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A5A* gene.

201. A method for increasing production of a dicarboxylic acid comprising:

a) providing a host cell having a naturally occurring number of *CYP52A5B* genes;

b) increasing, in the host cell, the number of *CYP52A5B* genes which encode a *CYP52A5B* protein having the amino acid sequence as set forth in SEQ ID NO: 101;

c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A5B* gene, to effect increased production of dicarboxylic acid.

202. A method for increasing the production of a *CYP52A5B* protein having an amino acid sequence as set forth in SEQ ID NO: 101 comprising:

a) transforming a host cell having a naturally occurring amount of *CYP52A5B* protein with an increased copy number of a *CYP52A5B* gene that encodes the *CYP52A5B* protein having the amino acid sequence as set forth in SEQ ID NO: 101; and

b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A5B* gene.

203. A method for increasing production of a dicarboxylic acid comprising:

a) providing a host cell having a naturally occurring number of *CYP52A8A* genes;

b) increasing, in the host cell, the number of *CYP52A8A* genes which encode a *CYP52A8A* protein having the amino acid sequence as set forth in SEQ ID NO: 102;

c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A8A* gene, to effect increased production of dicarboxylic acid.

204. A method for increasing the production of a *CYP52A8A* protein having an amino acid sequence as set forth in SEQ ID NO: 102 comprising:

a) transforming a host cell having a naturally occurring amount of *CYP52A8A* protein with an increased copy number of a *CYP52A8A* gene that encodes the *CYP52A8A* protein having the amino acid sequence as set forth in SEQ ID NO: 102; and

b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A8A* gene.

205. A method for increasing production of a dicarboxylic acid comprising:

a) providing a host cell having a naturally occurring number of *CYP52A8B* genes;

b) increasing, in the host cell, the number of *CYP52A8B* genes which encode a *CYP52A8B* protein having the amino acid sequence as set forth in SEQ ID NO: 103;

c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52A8B* gene, to effect increased production of dicarboxylic acid.

206. A method for increasing the production of a *CYP52A8B* protein having an amino acid sequence as set forth in SEQ ID NO: 103 comprising:

a) transforming a host cell having a naturally occurring amount of *CYP52A8B* protein with an increased copy number of a *CYP52A8B* gene that encodes the *CYP52A8B* protein having the amino acid sequence as set forth in SEQ ID NO: 103; and

b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52A8B* gene.

207. A method for increasing production of a dicarboxylic acid comprising:

a) providing a host cell having a naturally occurring number of *CYP52D4A* genes;

b) increasing, in the host cell, the number of *CYP52D4A* genes which encode a *CYP52D4A* protein having the amino acid sequence as set forth in SEQ ID NO: 104;

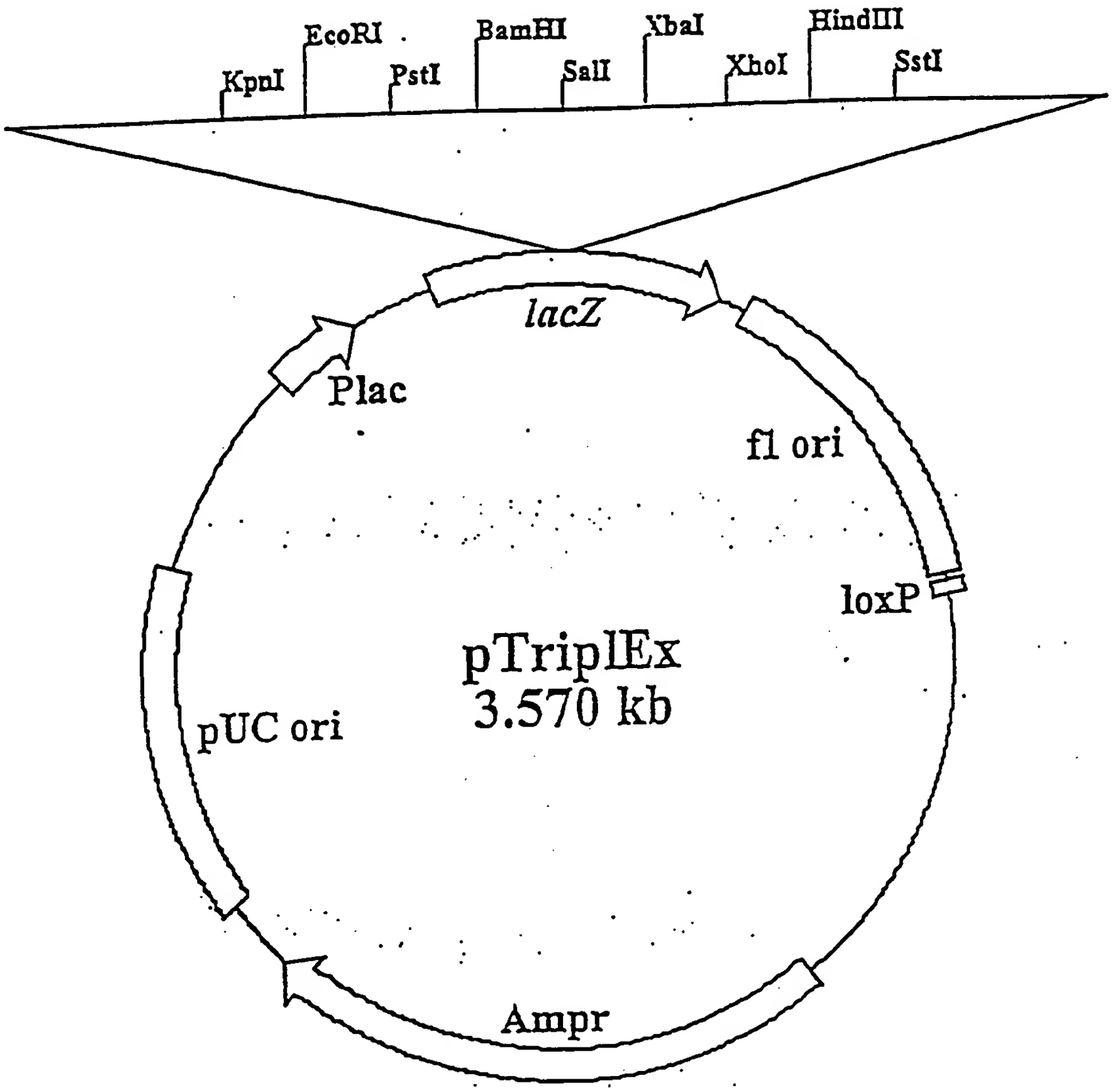
c) culturing the host cell in media containing an organic substrate which upregulates the *CYP52D4A* gene, to effect increased production of dicarboxylic acid.

208. A method for increasing the production of a *CYP52D4A* protein having an amino acid sequence as set forth in SEQ ID NO: 104 comprising:

a) transforming a host cell having a naturally occurring amount of *CYP52D4A* protein with an increased copy number of a *CYP52D4A* gene that encodes the *CYP52D4A* protein having the amino acid sequence as set forth in SEQ ID NO: 104; and

b) culturing the cell and thereby increasing expression of the protein compared with that of a host cell containing a naturally occurring copy number of the *CYP52D4A* gene.

209. A method for discriminating members of a gene family according to claim 181 wherein culturing the organism with the organic substrate is accomplished in a fermentor.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EcoRI
PstI
BamHI
SalI
XbaI
XhoI
HindIII
SstI
lacZ
Plac
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loxP
pTriplEx
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pUC ori
Ampr

Figure 1

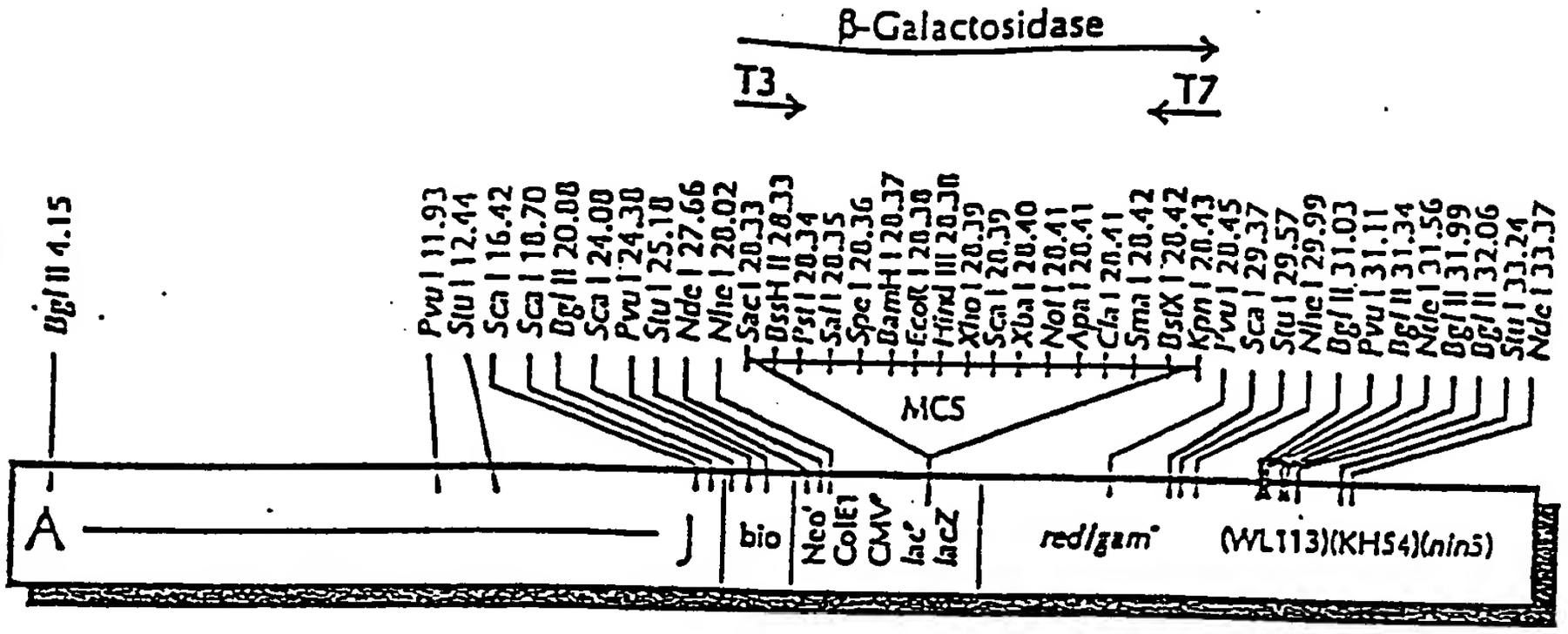


Figure 2A

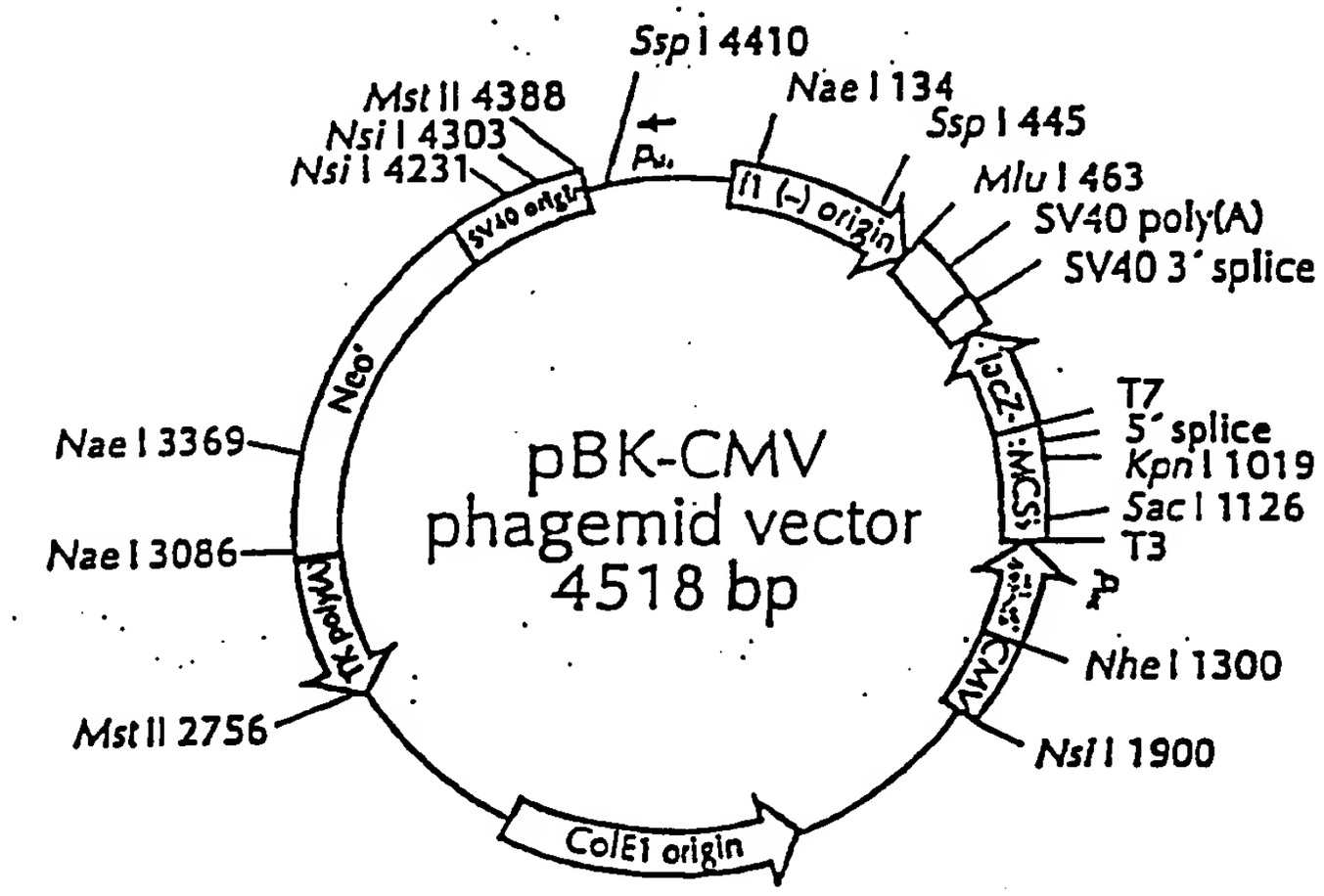


Figure 2B

QC-RT-PCR primers for the 5' coding sequence of *Candida tropicalis* 20336 P450*CYP52A5A*

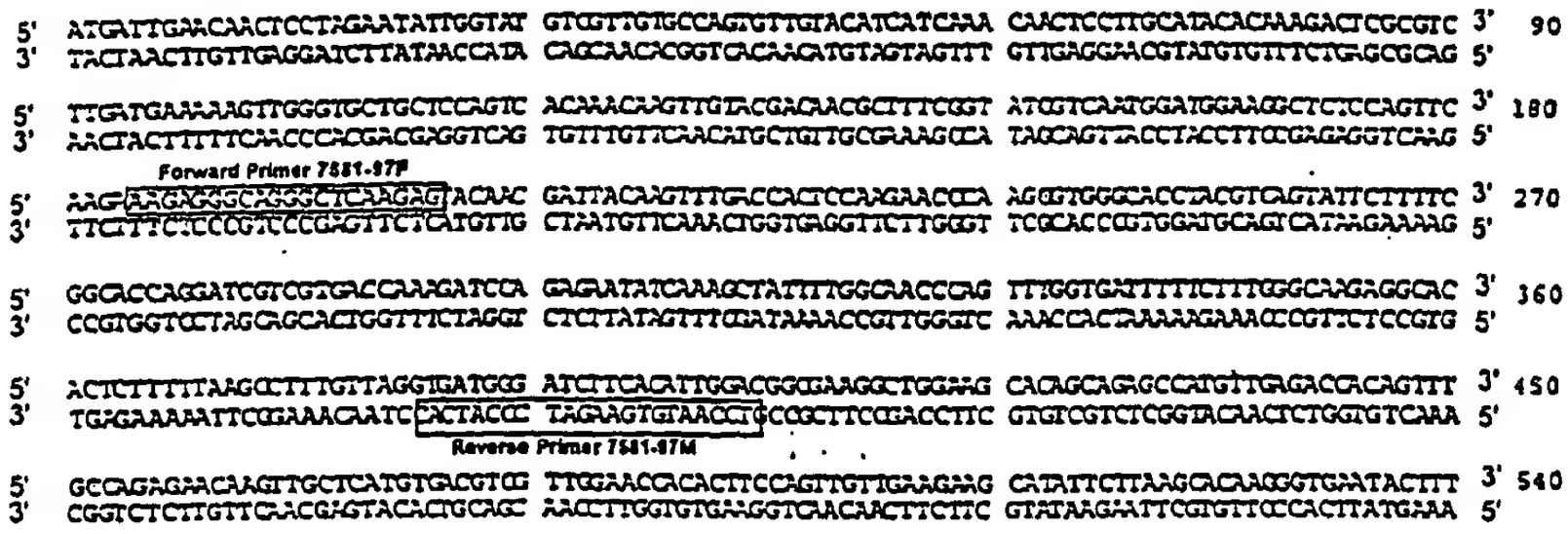


Figure 3

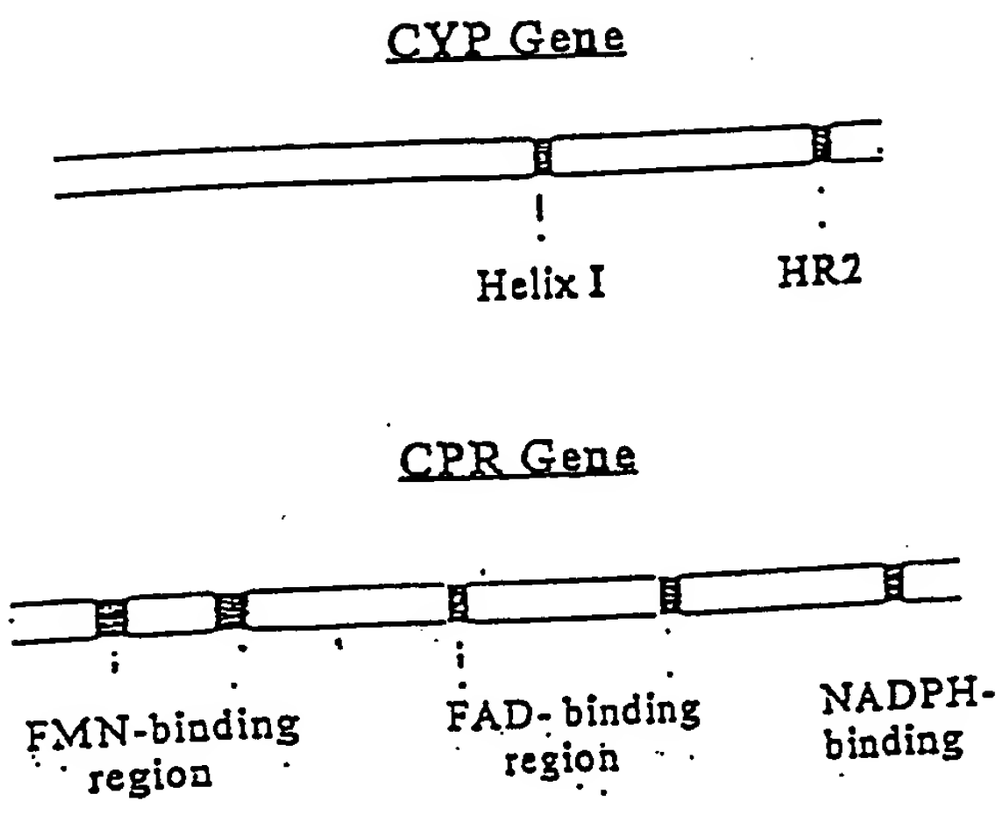
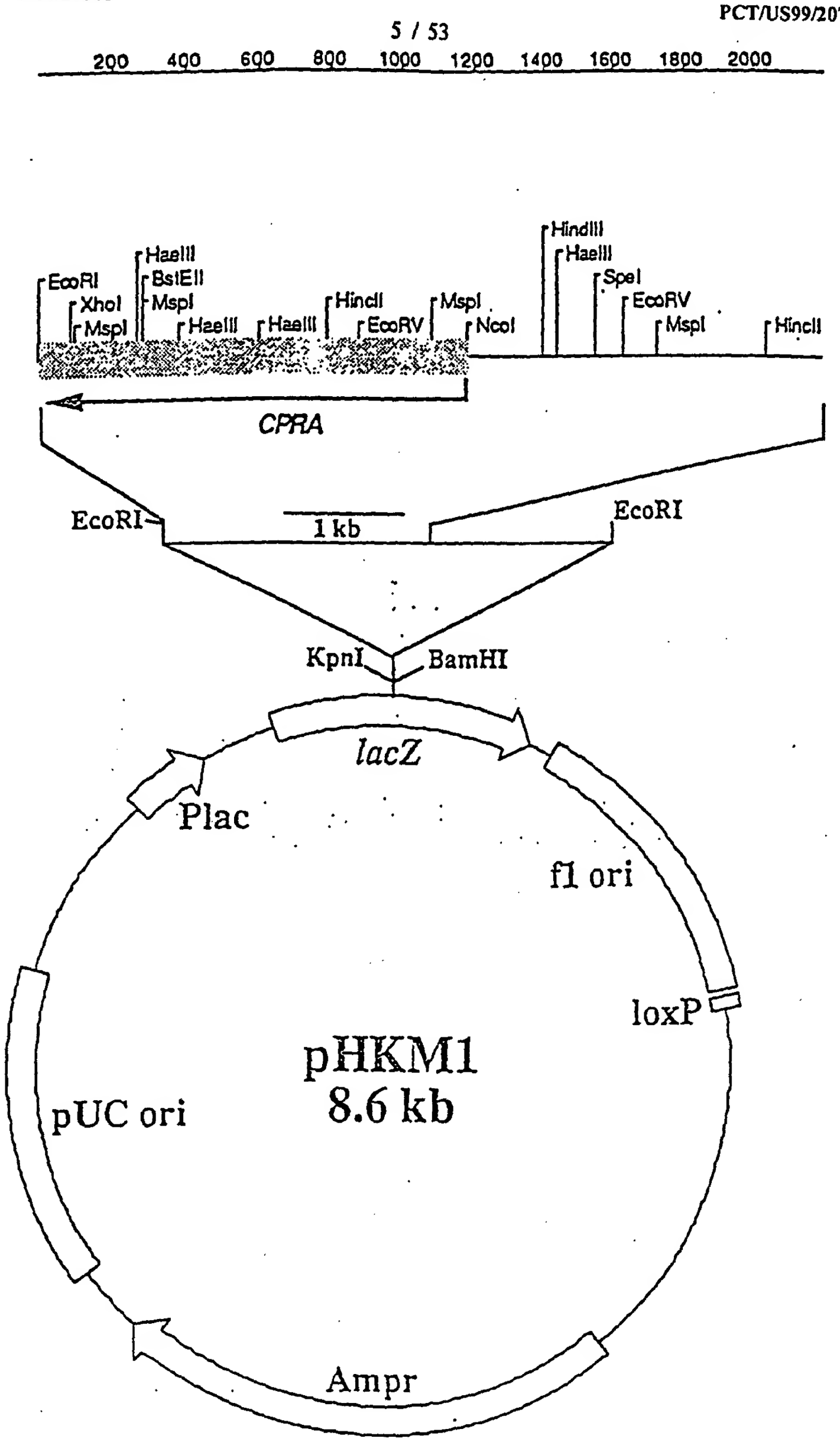

CYP Gene
Helix I
HR2
CPR Gene
FMN-binding region
FAD- binding region
NADPH-binding

Figure 4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400
600
800
1000
1200
1400
1600
1800
2000
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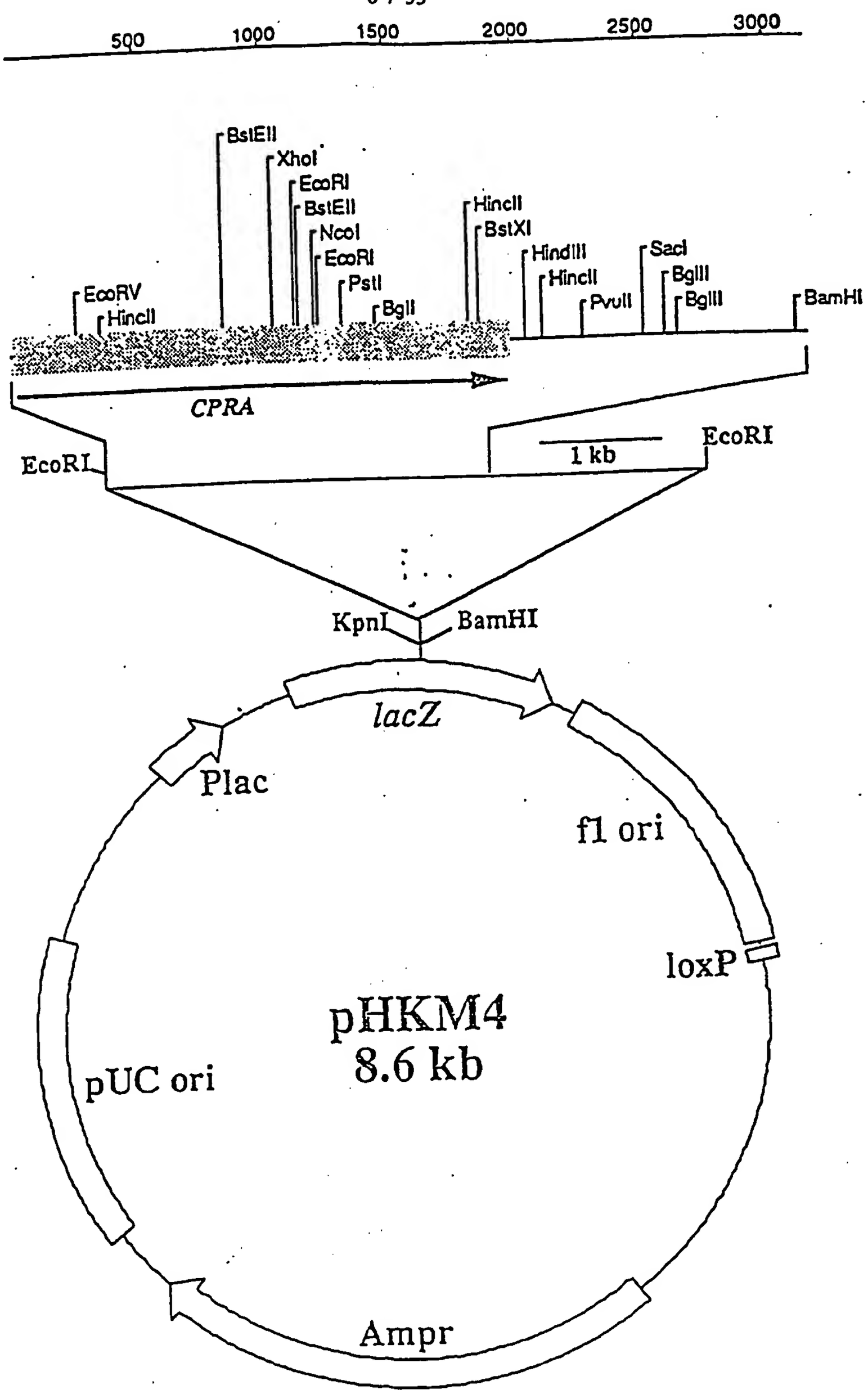
XhoI
MspI
HaeIII
BstEII
MspI
HaeIII
HaeIII
HincII
EcoRV
MspI
NcoI
HindIII
HaeIII
SpeI
EcoRV
MspI
HincII
CPRA
EcoRI
1 kb
EcoRI
KpnI
BamHI
lacZ
Plac
f1 ori
loxP
pHKM1
8.6 kb
pUC ori
Ampr

Figure 5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1500
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2500
3000
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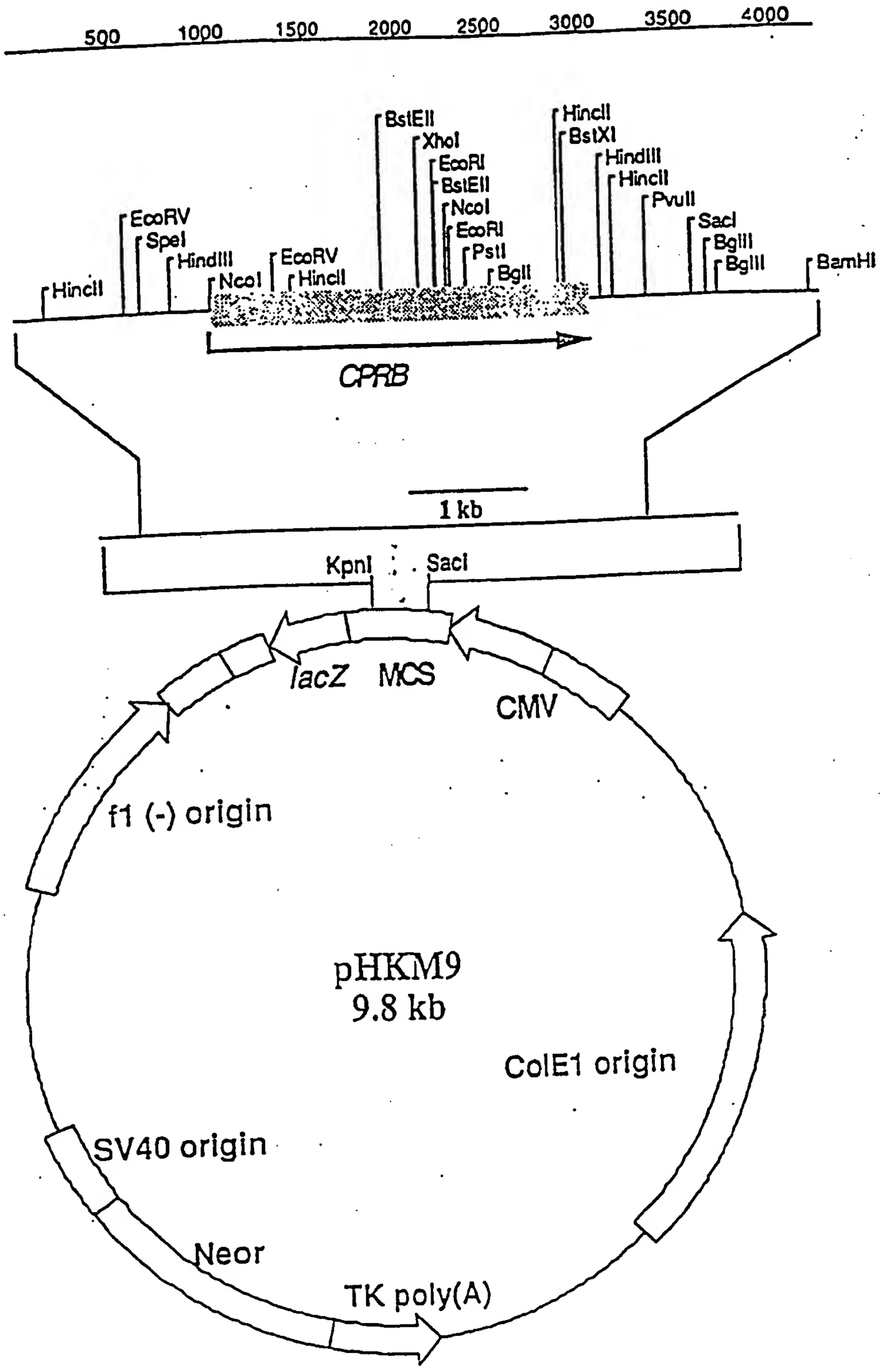
XhoI
EcoRI
BstEII
NcoI
EcoRI
PstI
BglI
EcoRV
HincII
HincII
BstXI
HindIII
HincII
PvuII
SacI
BglII
BglII
BamHI
CPRA
EcoRI
1 kb
EcoRI
KpnI
BamHI
lacZ
Plac
f1 ori
loxP
pHKM4
8.6 kb
pUC ori
Ampr

Figure 6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2500
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3500
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EcoRV
SpeI
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NcoI
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HincII
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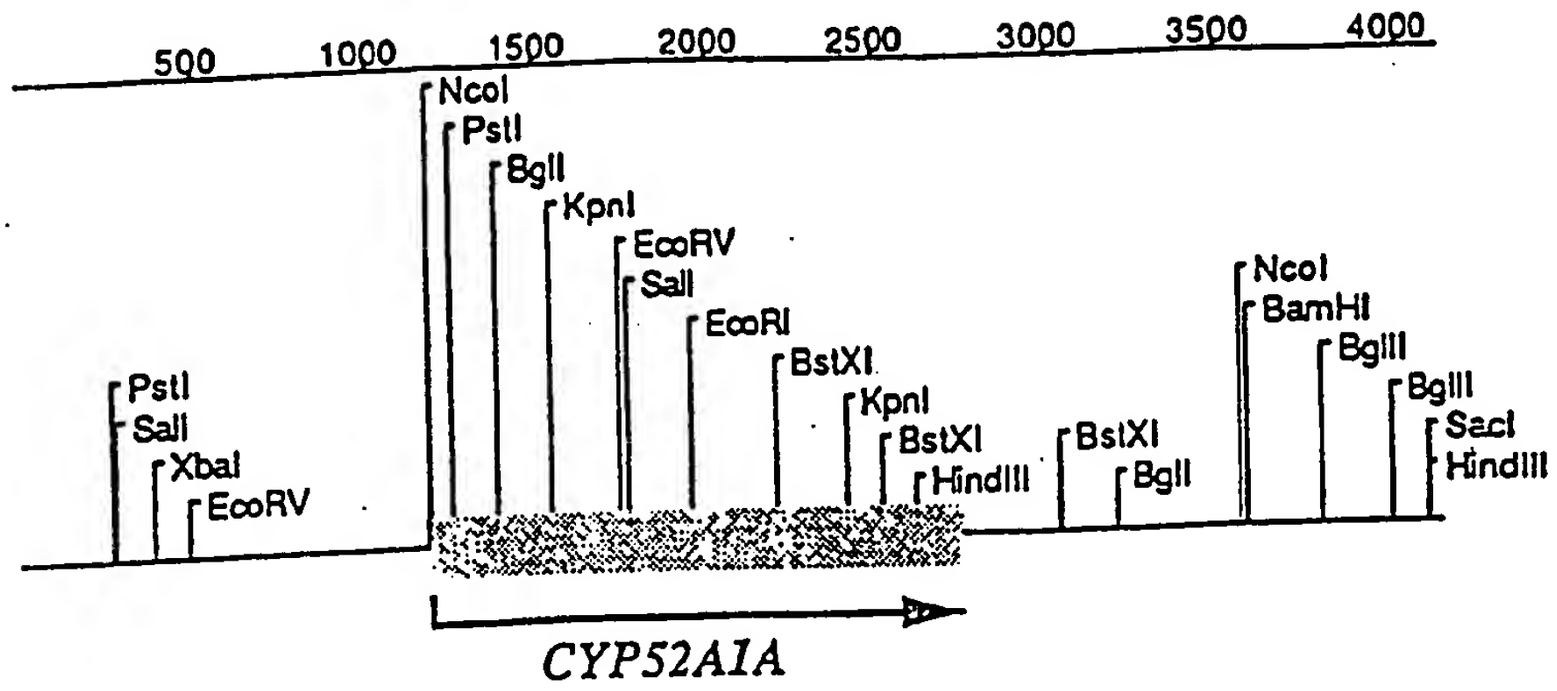
XhoI
EcoRI
BstEII
NcoI
EcoRI
PstI
BglI
HincII
BstXI
HindIII
HincII
PvuII
SacI
BglII
BglII
BamHI
CPRB
1 kb
KpnI
SacI
lacZ
MCS
CMV
f1 (-) origin
pHKM9
9.8 kb
ColE1 origin
SV40 origin
Neor
TK poly(A)

Figure 7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KpnI
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EcoRI
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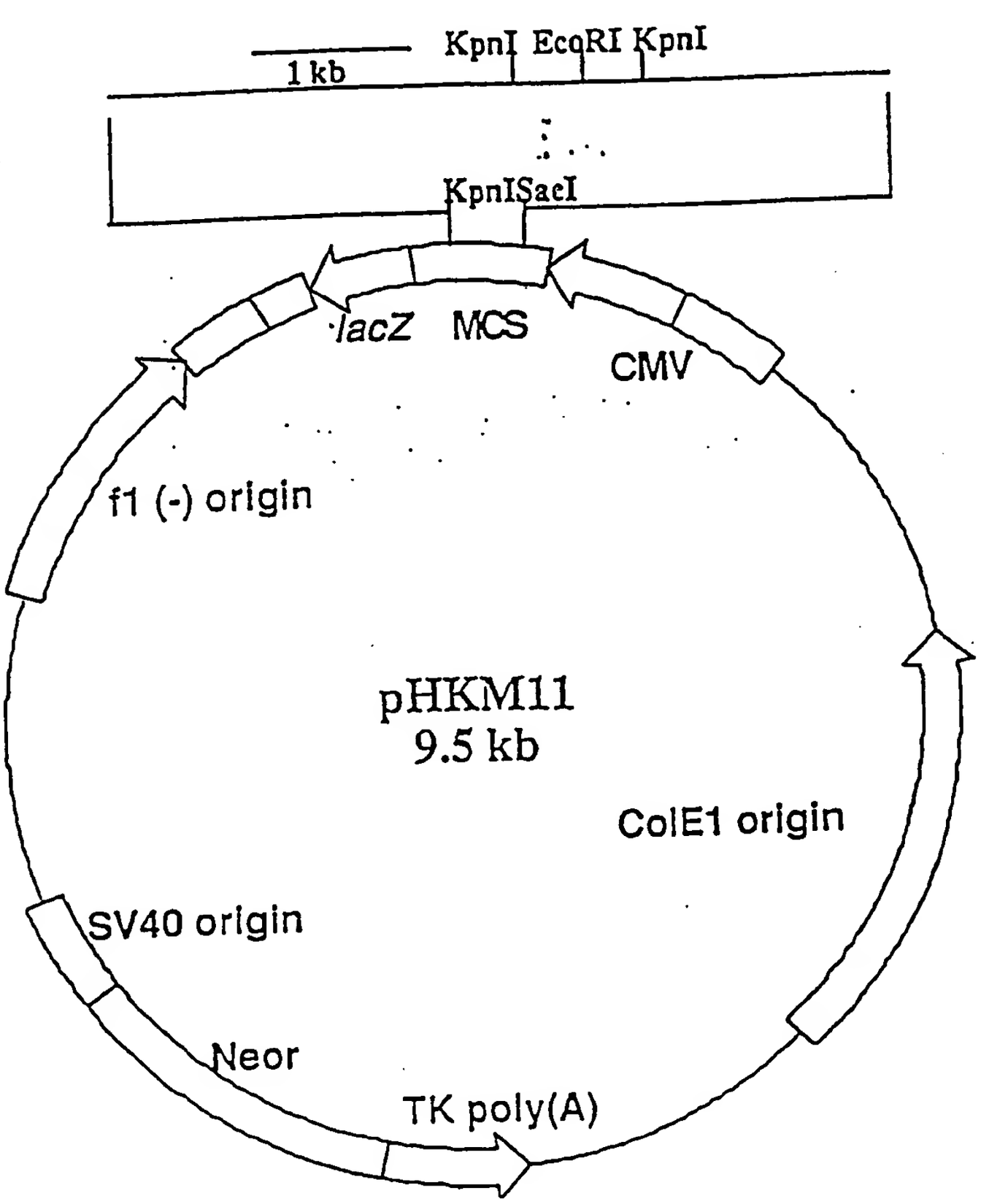
KpnI
BstXI
HindIII
PstI
SalI
XbaI
EcoRV
BstXI
BglI
NcoI
BamHI
BglII
BglII
SacI
HindIII
CYP52A1A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KpnISacI
lacZ
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CMV
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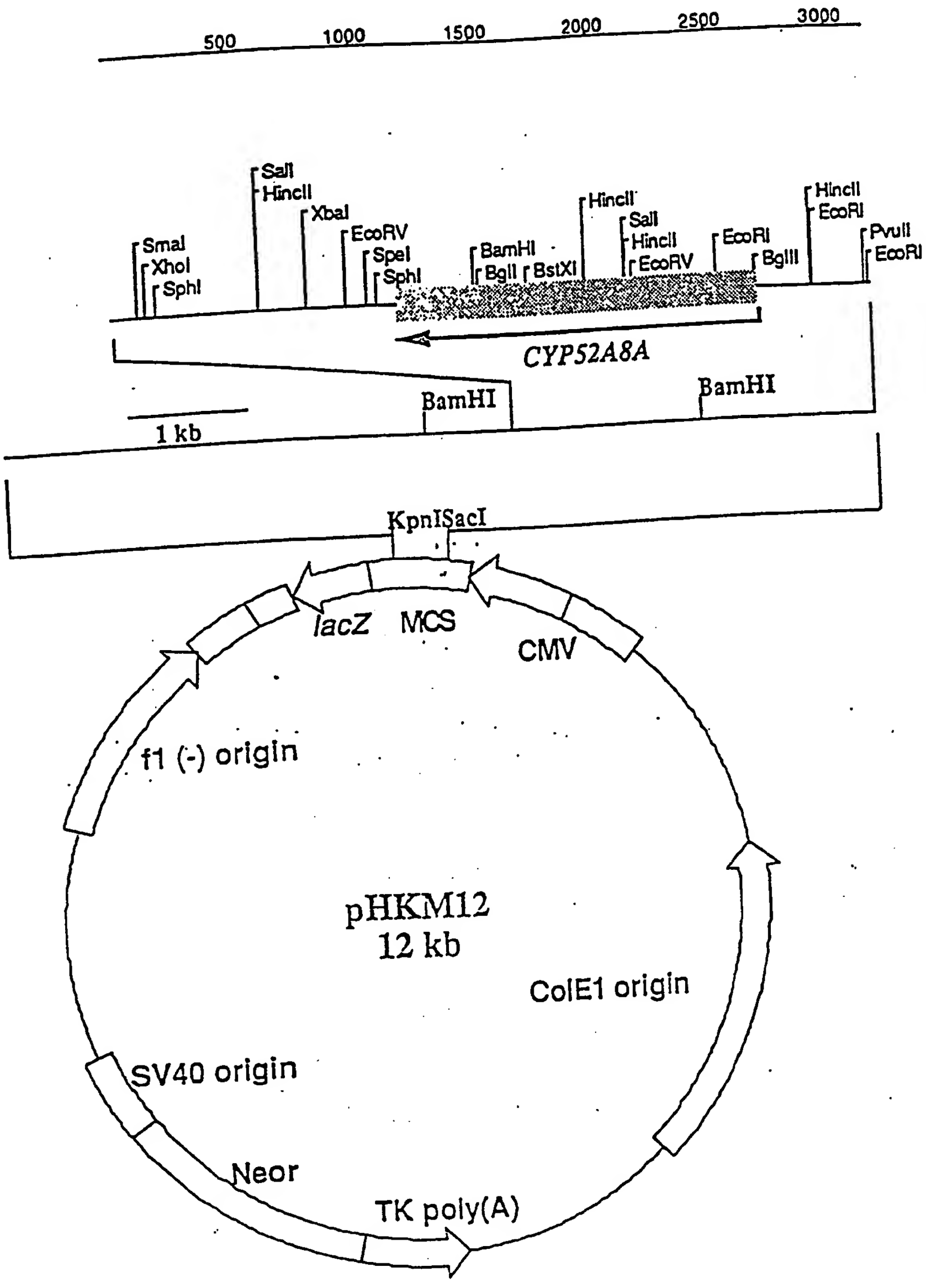
pHKM11
9.5 kb
ColE1 origin
SV40 origin
Neor
TK poly(A)

Figure 8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1500
2000
2500
3000
SmaI
XhoI
SphI
SalI
HincII
XbaI
EcoRV
SpeI
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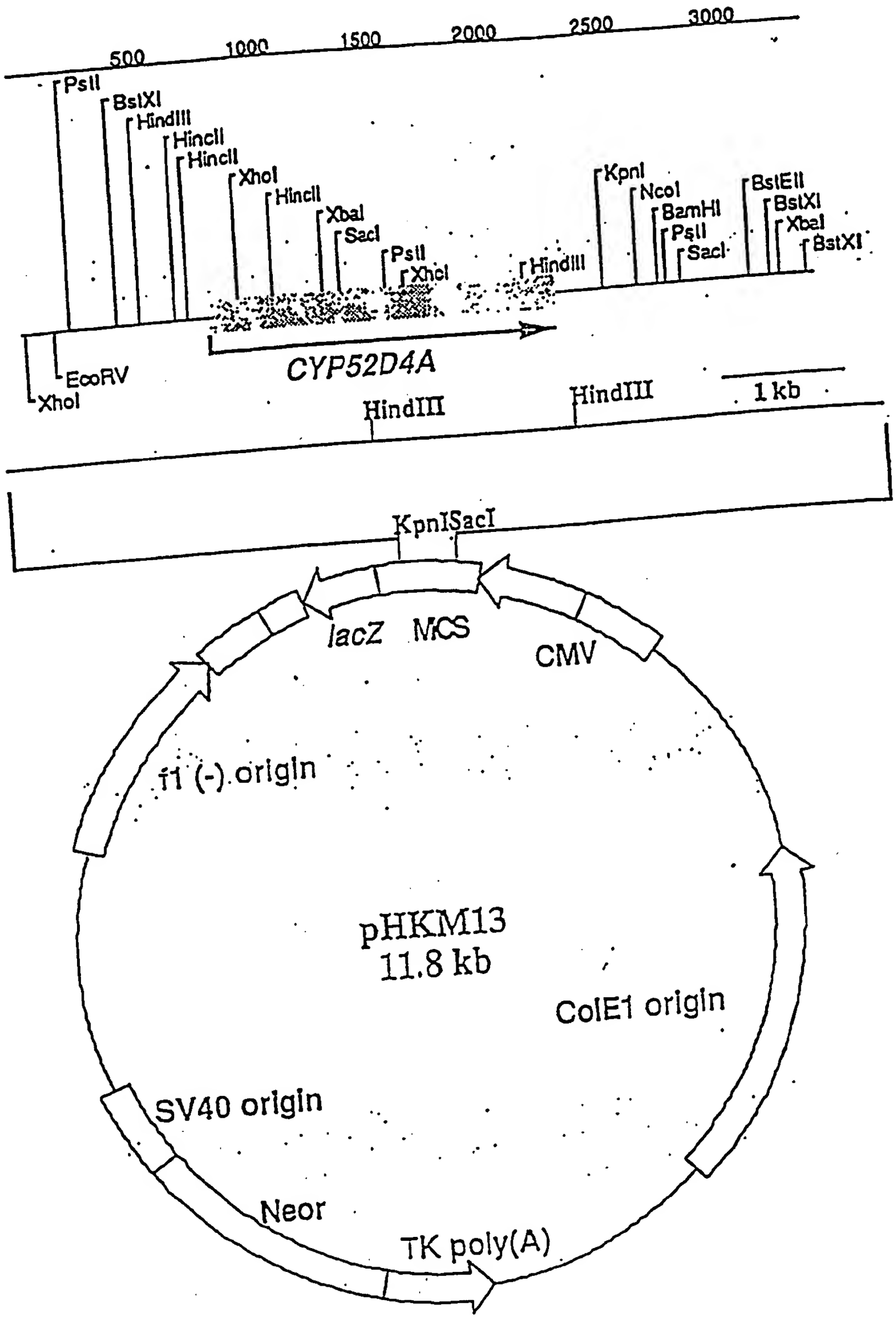
BglI
BstXI
HincII
SalI
HincII
EcoRV
EcoRI
BglII
HincII
EcoRI
PvuII
EcoRI
CYP52A8A
BamHI
BamHI
1 kb
KpnISacI
lacZ
MCS
CMV
f1 (-) origin
pHKM12
12 kb
ColE1 origin
SV40 origin
Neor
TK poly(A)

Figure 9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2000
2500
3000
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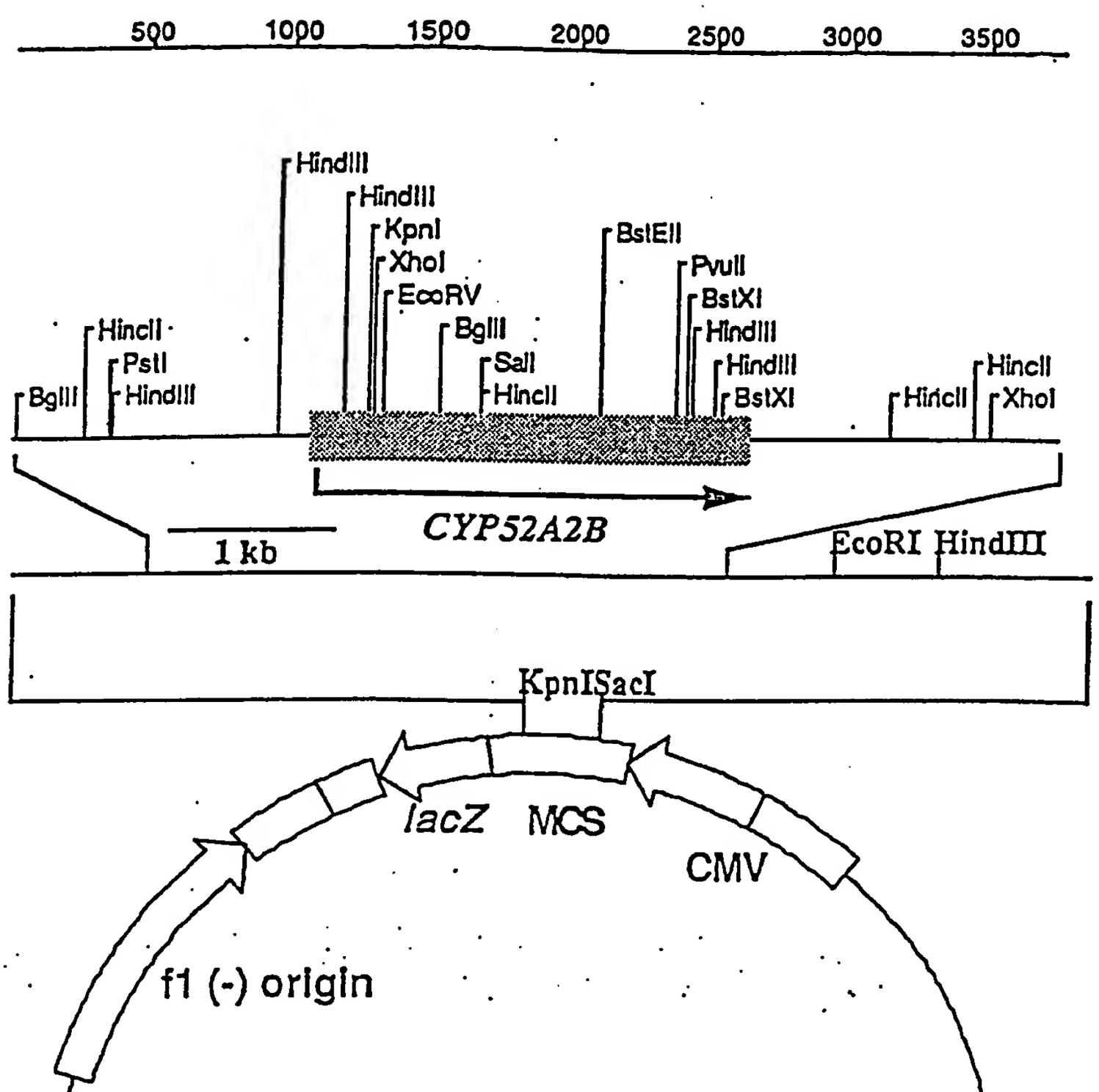
BstXI
HindIII
HincII
HincII
XhoI
HincII
XbaI
SacI
PstI
XhoI
HindIII
KpnI
NcoI
BamHI
PstI
SacI
BstEII
BstXI
XbaI
BstXI
CYP52D4A
EcoRV
XhoI
1 kb
HindIII
HindIII
KpnI
SacI
lacZ
MCS
CMV
f1 (-) origin
pHKM13
11.8 kb
ColE1 origin
SV40 origin
Neor
TK poly(A)

Figure 10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2000
2500
3000
3500
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XhoI
EcoRV
BglII
SalI
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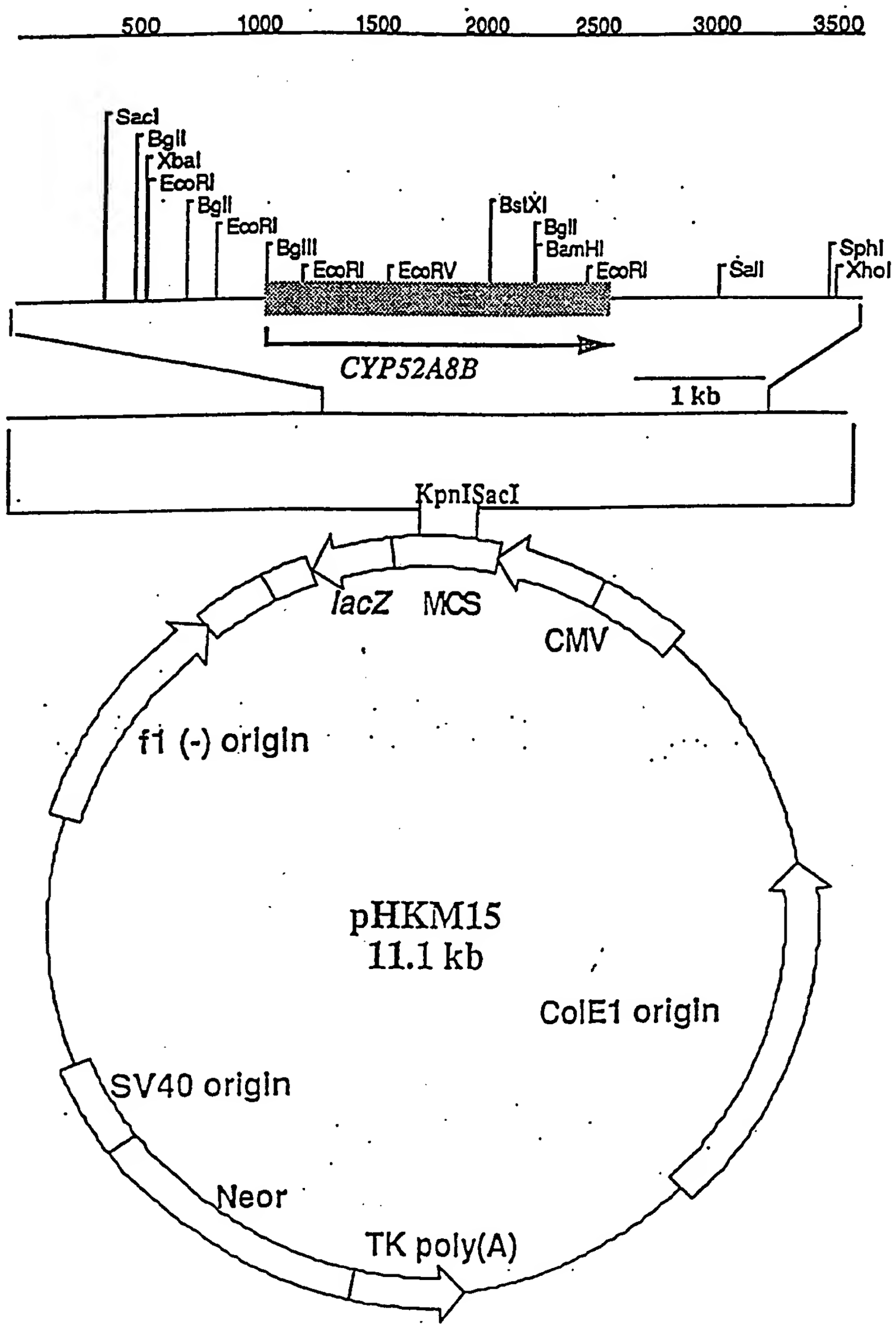
PvuII
BstXI
HindIII
HindIII
BstXI
BglII
HincII
PstI
HindIII
HincII
XhoI
CYP52A2B
1 kb
EcoRI HindIII
KpnISacI
lacZ
MCS
CMV
f1 (-) origin
pHKM14
11.3 kb
ColE1 origin
SV40 origin
Neor
TK poly(A)

Figure 11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2500
3000
3500
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BglI
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BglI
EcoRI
BglII
EcoRI
EcoRV
BstXI
BglI
BamHI
EcoRI
SalI
SphI
XhoI
CYP52A8B
1 kb
KpnISacI
lacZ
MCS
CMV
f1 (-) origin
pHKM15
11.1 kb
ColE1 origin
SV40 origin
Neor
TK poly(A)

Figure 12

C. tropicalis 20336 *CPR* Allele DNA Alignment of DS Sequence

```
                                                                           CATCA     5
CPRA      1
CPRB      1 TATATGATATATGATATATCTTCCTGTGTAATTATTATTCGTATTCGTTAATACTTACTACATTTTTTTT    70
                                                                               *

CPRA      6 AGATCATCTATGGGGATAATTA-----CGACAGCAACATTGCAGAAAGAGCGTTGGTCACAATCGAAAGA    70
CPRB     71 TCTTTATTTATGAAGAAAAGGAGAGTTCGTAAGTTGAGTTGAGTAGAATAGGCTGTTGTGCATACGGGGA   140
              * ** ****  ** **  *      **  **      ***   * *    * ** *     **     **

CPRA     71 GCCTATG-GCGTTGCCGTCGTTGAGGCAAATGACAGCAC--CAACAATAACGATGGTCCCAGTGAAGAGC   137
CPRB    141 GCAGAGGAGAGTATCCGACGAGGAGGAACTGGGTGAAATTTCATCTATGCTGTTGCGTCCTGTACTGTAC   210
            **   * * * **  *** **  **** *     *     *     ** * **   * **   ** **    *  *

CPRA    138 CTTCAGAACAGTCCATTGTTGACGCT--TAAGGCACGGATAATTACGTGGGGCAAAGGAACGCGGAATTA   205
CPRB    211 TGTAAATCTTAGATTTCCTAGAGGTTGTTCTAGCAAATAAAGTGTTTCAAGATACAATTTTACAGGCAAG   280
              * *            * * ** * *  *    ***    * * *           *  * *      * *

CPRA    206 GTTATGGGGGGATCAAA--AGCGGAAGATTTGTGTTGCTTGTGGGTTTTTTCCTTTATTTTTCATATGAT   273
CPRB    281 GGTAAAGGATCAACTGATTAGCGGAAGATTGGTGTTGCCTGTGGGGTTCTT---TTATTTTTCATATGAT   347
            * **  **   * *  * *********** ******* ****** ** **   ****************

CPRA    274 TTCTTTGCGCAAGTAACATGTGCCAATTTAGTTTGTGATTAGCGTGCC-CCACAATTGGCATCGTGGACG   342
CPRB    348 TTCTTTGCGCGAGTAACATGTGCCAATCTAGTTTATGATTAGCGTACCTCCACAATTGGCATCTTGGACG   417
            ********** **************** ****** ********** ** ************** ******

CPRA    343 GGCGTGTTTTGTCATACCCCAAGTCTTAACTAGCTCCACAGTCTCGACGGTGTCTCGACGATGTCTTCTT   412
CPRB    418 GGCGTGTTTTGTCTTACCCCAAGCCTTATTTAGTTCCACAGTCTCGACGGTGTCTCGCCGATGTCTTCTC   487
            ************* ********* ****  *** ********************** ***********

CPRA    413 CCACCCCTCCCATGAATCATTCAAAGTTGTTGGGGGATCTCCACCAAGGGCACCGGAGTTAATGCTTATG   482
CPRB    488 CCACCCCTCGCAGGAATCATTCGAAGTTGTTGGGGGATCTCCTCC---------GCAGTTTATGTTCATG   548
            ********* ** ********* ******************* **         * **** *** * ***

CPRA    483 TTTCTCCCACTTTGGTTGTGATTGGGGTAGTCTAGTGAGTTGGAGATTTTCTTTTTTTCGCAGGTGTCTC   552
CPRB    549 TCTTTCCCACTTTGGTTGTGATTGGGGTAGCGTAGTGAGTTGGTGATTTTCTTTTTT-CGCAGGTGTCTC   617
            * * **************************  *********** ************* ************

CPRA    553 CGATATCGAAATTTGATGAATATAGAGAGAAGCCAGATCAGCACAGTAGATTGCCTTTGTAGTTAGAGAT   622
CPRB    618 CGATATCGAAGTTTGATGAATATAG----GAGCCAGATCAGCATGGTATATTGCCTTTGTAGATAGAGAT   683
            ********** **************     ************** *** ************* *******

CPRA    623 GTTGAACAGCAACTAGTTGAATTACACGCCACCACTTGACAGCAAGTGCAGTGAGCTGTAAACGATGCAG   692
CPRB    684 GTTGAACAACAACTAGCTGAATTACACACCACCGCT----------------------AAACGATGCGC   730
            ******** ******* ********** ***** **                      *********

CPRA    693 CCAGAGTGTCACCACCAACTGACGTTGGGTGGAGTTGTTGTTGTTGTTGTTGGCAGGGCCATATTGCTAA   762
CPRB    731 ACAGGGTGTCACCGCCAACTGACGTTGGGTGGAGTTG---------TTGTTGGCAGGGCCATATTGCTAA   791
             *** ******** ***********************          ************************

CPRA    763 ACGAAGACAAGTAGCACAAAACCCAAGCTTAAGAACAAAAATAAAAAAAATTCATACGACAATTCCAAAG   832
CPRB    792 ACGAAGAGAAGTAGCACAAAACCCAAGGTTAAGAACAA---TTAAAAAAATTCATACGACAATTCCACAG   858
            ******* ******************* **********    * ************************ **

CPRA    833 CCATTGATTTACATAAT--CAACAG-TAAGACAGAAAAAACTTTCAACATTTCAAAGTTCCCTTTTTCCT   899
CPRB    859 CCATTTACATAATCAACAGCGACAAATGAGACAGAAAAAACTTTCAACATTTCAAAGTTCCCTTTTTCCT   928
            ***** *  **   **   * ***  * **************************************

CPRA    900 ATTACTTCTTTTTTTTCTTCTTTCCTT-------CTTTCCTTCTGTTTTTCTTACTTTATCAGTCTTTTA   962
CPRB    929 ATTACTTCTTTTTTTCTTTCCTTCCTTTCATTTCCTTTCCTTCTGCTTTTATTACTTTACCAGTCTTTTG   998
            ***************  *** ******        *********** **** ******** *********

CPRA    953 CTTGTTTTTGCAATTCCTCATCCTCCTCCTACTCCTCCTCACCATGGCTTTAGACAAGTTAGATTTGTAT  1032
CPRB    999 CTTGTTTTTGCAATTCCTCATCCTCCTCCT---------CACCATGGCTTTAGACAAGTTAGATTTGTAT  1059
            ******************************         *******************************
```

Figure 13A

```
CPRA  1033 GTCATCATAACATTGGTGGTCGCTGTAGCCGCCTATTTTGCTAAGAACCAGTTCCTTGATCAGCCCCAGG 1102
CPRB  1060 GTCATCATAACATTGGTGGTCGCTGTGGCCGCCTATTTTGCTAAGAACCAGTTCCTTGATCAGCCCCAGG 1129
           ************************* ************************************************

CPRA  1103 ACACCGGGTTCCTCAACACGGACAGCGGAAGCAACTCCAGAGACGTCTTGCTGACATTGAAGAAGAATAA 1172
CPRB  1130 ACACCGGGTTCCTCAACACGGACAGCGGAAGCAACTCCAGAGACGTCTTGCTGACATTGAAGAAGAATAA 1199
           ************************************************************************

CPRA  1173 TAAAAACACGTTGTTGTTGTTTGGGTCCCAGACGGGTACGGCAGAAGATTACGCCAACAAATTGTCCAGA 1242
CPRB  1200 TAAAAACACGTTGTTGTTGTTTGGGTCCCAGACCGGTACGGCAGAAGATTACGCCAACAAATTGTCAAGA 1269
           ********************************* ********************************** ***

CPRA  1243 GAATTGCACTCCAGATTTGGCTTGAAAACGATGGTTGCAGATTTCGCTGATTACGATTGGGATAACTTCG 1312
CPRB  1270 GAATTGCACTCCAGATTTGGCTTGAAAACCATGGTTGCAGATTTCGCTGATTACGATTGGGATAACTTCG 1339
           ***************************** ************************************

CPRA  1313 GAGATATCACCGAAGACATCTTGGTGTTTTTCATTGTTGCCACCTATGGTGAGGGTGAACCTACCGATAA 1382
CPRB  1340 GAGATATCACCGAAGATATCTTGGTGTTTTTCATCGTTGCCACCTACGGTGAGGGTGAACCTACCGACAA 1409
           ********** ********** ********** ********** ********** ********** **

CPRA  1383 TGCCGACGAGTTCCACACCTGGTTGACTGAAGAAGCTGACACTTTGAGTACCTTGAAATACACCGTGTTC 1452
CPRB  1410 TGCCGACGAGTTCCACACCTGGTTGACTGAAGAAGCTGACACTTTGAGTACTTTGAGATATACCGTGTTC 1479
           ************************************************** **** *** *********

CPRA  1453 GGGTTGGGTAACTCCACGTACGAGTTCTTCAATGCCATTGGTAGAAAGTTTGACAGATTGTTGAGCGAGA 1522
CPRB  1480 GGGTTGGGTAACTCCACCTACGAGTTCTTCAATGCTATTGGTAGAAAGTTTGACAGATTGTTGAGTGAGA 1549
           ********** ********** ********** ********** ********** ********** ****

CPRA  1523 AAGGTGGTGACAGGTTTGCTGAATACGCTGAAGGTGATGACGGTACTGGCACCTTGGACGAAGATTTCAT 1592
CPRB  1550 AAGGTGGTGACAGATTTGCTGAATATGCTGAAGGTGACGACGGCACTGGCACCTTGGACGAAGATTTCAT 1619
           ********** ********** ********** ********** ********** ********** ******

CPRA  1593 GGCCTGGAAGGACAATGTCTTTGACGCCTTGAAGAATGATTTGAACTTTGAAGAAAAGGAATTGAAGTAC 1662
CPRB  1620 GGCCTGGAAGGATAATGTCTTTGACGCCTTGAAGAATGACTTGAACTTTGAAGAAAAGGAATTGAAGTAC 1689
           ********** ********** ********** ********** ********** ********** ******

CPRA  1663 GAACCAAACGTGAAATTGACTGAGAGAGACGACTTGTCTGCTGCTGACTCCCAAGTTTCCTTGGGTGAGC 1732
CPRB  1690 GAACCAAACGTGAAATTGACTGAGAGAGATGACTTGTCTGCTGCCGACTCCCAAGTTTCCTTGGGTGAGC 1759
           ********** ********** ********** ********** ********** ********** ******

CPRA  1733 CAAACAAGAAGTACATCAACTCCGAGGGCATCGACTTGACCAAGGGTCCATTCGACCACACCCACCCATA 1802
CPRB  1760 CAAACAAGAAGTACATCAACTCCGAGGGCATCGACTTGACCAAGGGTCCATTCGACCACACCCACCCATA 1829
           ************************************************************************

CPRA  1803 CTTGGCCAGAATCACCGAGACGAGAGAGTTGTTCAGCTCCAAGGACAGACACTGTATCCACGTTGAATTT 1872
CPRB  1830 CTTGGCCAGGATCACCGAGACCAGAGAGTTGTTCAGCTCCAAGGAAAGACACTGTATTCACGTTGAATTT 1899
           ********* ********** ********** ********** ********** ********** ******

CPRA  1873 GACATTTCTGAATCGAACTTGAAATACACCACCGGTGACCATCTAGCTATCTGGCCATCCAACTCCGACG 1942
CPRB  1900 GACATTTCTGAATCGAACTTGAAATACACCACCGGTGACCATCTAGCCATCTGGCCATCCAACTCCGACG 1969
           ************************************************** ********************

CPRA  1943 AAAACATTAAGCAATTTGCCAAGTGTTTCGGATTGGAAGATAAACTCGACACTGTTATTGAATTGAAGGC 2012
CPRB  1970 AAAACATCAAGCAATTTGCCAAGTGTTTCGGATTGGAAGATAAACTCGACACTGTTATTGAATTGAAGGC 2039
           ******* ********************************************************************

CPRA  2013 GTTGGACTCCACTTACACCATCCCATTCCCAACCCCAATTACCTACGGTGCTGTCATTAGACACCATTTA 2082
CPRB  2040 ATTGGACTCCACTTACACCATTCCATTCCCAACTCCAATTACTTACGGTGCTGTCATTAGACACCATTTA 2109
           ******************** ********** ******** ************************** 

CPRA  2083 GAAATCTCCGGTCCAGTCTCGAGACAATTCTTTTTGTCAATTGCTGGGTTTGCTCCTGATGAAGAAACAA 2152
CPRB  2110 GAAATCTCCGGTCCAGTCTCGAGACAATTCTTTTTGTCGATTGCTGGGTTTGCTCCTGATGAAGAAACAA 2179
           ************************************ ******************************

CPRA  2153 AGAAGGCTTTTACCAGACTTGGTGGTGACAAGCAAGAATTCGCCGCCAAGGTCACCCGCAGAAAGTTCAA 2222
CPRB  2180 AGAAGACTTTCACCAGACTTGGTGGTGACAAACAAGAATTCGCCACCAAGGTTACCCGCAGAAAGTTCAA 2249
           ***** **** ******************** *********** ******* ****************
```

Figure 13B

```
CPRA  2223 CATTGCCGATGCCTTGTTATATTCCTCCAACAACGCTCCATGGTCCGATGTTCCTTTTGAATTCCTTATT 2292
CPRB  2250 CATTGCCGATGCCTTGTTATATTCCTCCAACAACACTCCATGGTCCGATGTTCCTTTTGAGTTCCTTATT 2319
           ********************************** ************************ *********

CPRA  2293 GAAAACGTTCCACACTTGACTCCACGTTACTACTCCATTTCGTCTTCGTCATTGAGTGAAAAGCAACTCA 2362
CPRB  2320 GAAAACATCCAACACTTGACTCCACGTTACTACTCCATTTCTTCTTCGTCGTTGAGTGAAAAACAACTCA 2389
           ****** * * ******************************** ******** ********** *******

CPRA  2363 TCAACGTTACTGCAGTTGTTGAAGCCGAAGAAGAAGCTGATGGCAGACCAGTCACTGGTGTTGTCACCAA 2432
CPRB  2390 TCAATGTTACTGCAGTCGTTGAGGCCGAAGAAGAAGCCGATGGCAGACCAGTCACTGGTGTTGTTACCAA 2459
           **** ********** ***** ************** ************************** *****

CPRA  2433 CTTGTTGAAGAACGTTGAAATTGTGCAAAACAAGACTGGCGAAAAGCCACTTGTCCACTACGATTTGAGC 2502
CPRB  2460 CTTGTTGAAGAACATTGAAATTGCGCAAAACAAGACTGGCGAAAAGCCACTTGTTCACTACGATTTGAGC 2529
           ************ ********* ******************************** ***************

CPRA  2503 GGCCCAAGAGGCAAGTTCAACAAGTTCAAGTTGCCAGTGCATGTGAGAAGATCCAACTTTAAGTTGCCAA 2572
CPRB  2530 GGCCCAAGAGGCAAGTTCAACAAGTTCAAGTTGCCAGTGCACGTGAGAAGATCCAACTTTAAGTTGCCAA 2599
           ************************************** ************************** 

CPRA  2573 AGAACTCCACCACCCCAGTTATCTTGATTGGTCCAGGTACTGGTGTTGCCCCATTGAGAGGTTTTGTCAG 2642
CPRB  2600 AGAACTCCACCACCCCAGTTATCTTGATTGGTCCAGGTACTGGTGTTGCCCCATTGAGAGGTTTCGTTAG 2669
           ************************************************************ ** **

CPRA  2643 AGAAAGAGTTCAACAAGTCAAGAATGGTGTCAATGTTGGCAAGACTTTGTTGTTTTATGGTTGCAGAAAC 2712
CPRB  2670 AGAAAGAGTTCAACAAGTCAAGAATGGTGTCAATGTTGGCAAGACTTTGTTGTTTTATGGTTGCAGAAAC 2739
           ************************************************************ *******

CPRA  2713 TCCAACGAGGACTTTTTGTACAAGCAAGAATGGGCCGAGTACGCTTCTGTTTTGGGTGAAAACTTTGAGA 2782
CPRB  2740 TCCAACGAGGACTTTTTGTACAAGCAAGAATGGGCCGAGTACGCTTCTGTTTTGGGTGAAAACTTTGAGA 2809
           ************************************************************ *******

CPRA  2783 TGTTCAATGCCTTCTCCAGACAAGACCCATCCAAGAAGGTTTACGTCCAGGATAAGATTTTAGAAAACAG 2852
CPRB  2810 TGTTCAATGCCTTCTCTAGACAAGACCCATCCAAGAAGGTTTACGTCCAGGATAAGATTTTAGAAAACAG 2879
           *************** ************************************************** 

CPRA  2853 CCAACTTGTGCACGAGTTGTTGACTGAAGGTGCCATTATCTACGTCTGTGGTGATGCCAGTAGAATGGCT 2922
CPRB  2880 CCAACTTGTGCACGAATTGTTGACCGAAGGTGCCATTATCTACGTCTGTGGTGACGCCAGTAGAATGGCC 2949
           *************** ******** ***************************** ************** 

CPRA  2923 AGAGACGTGCAGACCACAATTTCCAAGATTGTTGCTAAAAGCAGAGAAATTAGTGAAGACAAGGCTGCTG 2992
CPRB  2550 AGAGACGTCCAGACCACGATCTCCAAGATTGTTGCCAAAAGCAGAGAAATCAGTGAAGACAAGGCCGCTG 3019
           ******** ******** ** ************** ************** ************** **** 

CPRA  2593 AATTGGTCAAGTCCTGGAAGGTCCAAAATAGATACCAAGAAGATGTTTGGTAGACTCAAACGAATCTCTC 3062
CPRB  3020 AATTGGTCAAGTCCTGGAAAGTCCAAAATAGATACCAAGAAGATGTTTGGTAGACTCAAACGAATCTCTC 3089
           ******************* ************************************************

CPRA  3063 TTTCTCCCAACGCATTTATGAATCTTTATTCTCATTGAAGCTTTACATATGTTCTACACTTTATTTTTTT 3132
CPRB  3090 TTTCTCCCAACGCATTTATGAA----TATTCTCATTGAAGTTTTACATATGTTCTATATTTCATTTTTTT 3155
           ********************    ************** ************** * ** ********

CPRA  3133 TTTTTTTTTTATTATTATATTACGAAACATAGGTCAACTATATATACTTGATTAAATGTTATAGAAACAA 3202
CPRB  3156 TTT----------ATTATATTACGAAACATAGGTCAACTATATATACTTGATTAAATGTTATAGAAACAA 3215
           ***          ************************************************************

CPRA  3203 TAACTATTATCTACTCGTCTACTTCTTTGGCATTGACATCAACATTACCGTTCCCATTACCGTTGCCGTT 3272
CPRB  3216 TAATTATTATCTACTCGTCTACTTCTTTGGCATTGGCATTGGCATTGGCATTGCCGTTGCCGTT 3285
           *** ******************************** *** . **** * ** **** ********** 

CPRA  3273 GGCAATGCCGGGATATTTAGTACAGTATCTCCAATCCGGATTTGAGCTATTGTAGATCAGCTGCAAGTCA 3342
CPRB  3286 GGTAATGCCGGGATATTTAGTACAGTATCTCCAATCCGGATTTGAGCTATTGTAAATCAGCTGCAAGTCA 3355
           ** ************************************************** ************** 

CPRA  3343 TTCTCCACCTTCAACCAGTACTTATACTTCATCTTTGACTTCAAGTCCAAGTCATAAATATTACAAGTTA 3412
CPRB  3356 TTCTCCACCTTCAACCAGTACTTATACTTCATCTTTGACTTCAAGTCCAAGTCATAAATATTACAAGTTA 3425
           ************************************************************ *******
```

Figure 13C

```
CPRA  3413 GCAAGAACTTCTGGCCATCCACGATATAGACGTTATTCACGTTATTATGCGACGTATGGATGTGGTTATC 3482
CPRB  3426 GCAAGAACTTCTGGCCATCCACAATATAGACGTTATTCACGTTATTATGCGACGTATGGATATGGTTATC 3495
           ********************** ************************************** ********

CPRA  3483 CTTATTGAACTTCTCAAACTTCAAAAACAACCCCACGTCCCGCAACGTCATTATCAACGACAAGTTCTGG 3552
CPRB  3496 CTTATTGAACTTCTCAAACTTCAAAAACAACCCCACGTCCCGCAACGTCATTATCAACGACAAGTTCTGA 3565
           ************************************************************************

CPRA  3553 CTCACGTCGTCGGAGCTCGTCAAGTTCTCAATTAGATCGTTCTTGTTATTGATCTTCTGGTACTTTCTCA 3622
CPRB  3566 CTCACGTCGTCGGAGCTCGTCAAGTTCTCAATTAGATCGTTCTTGTTATTGATCTTCTGGTACTTTCTCA 3635
           ************************************************************************

CPRA  3623 ATTGCTGGAACACATTGTCCTCGTTGTTCAAATAGATCTTGAACAACTTTTTCAACGGGATCAACTTCTC 3692
CPRB  3636 ACTGCTGGAACACATTGTCCTCGTTGTTCAAATAGATCTTGAACAACTTCTTCAAGGGAATCAACTTTTC 3705
           * ********************************************** ***** ** ******** **

CPRA  3693 AATCTGGGCCAAGATCTCCGCCGGGATCTTCAGAAACAAGTCCTGCAACCCCTGGTCGATGGTCTCCGGG 3762
CPRB  3706 GATCTGGGCCAAGATTTCCGCCGGGATCTTCAGAAACAAGTCCTGCAACCCCTGGTCGATGGTCTCGGGG 3775
           ************** ************************************************** ***

CPRA  3763 TACAACAAGTCCAAGGGGCAGAAGTGTCTAGGCACGTGTTTCAACTGGTTCAACGAACATGTTCGACAGT 3832
CPRB  3776 TACAACAAGTCTAAGGGGCAGAAGTGTCTAGGCACGTGTTTCAACTGGTTCAAGGAACATGTTCGACAGT 3845
           *********** ****************************************** ****************

CPRA  3833 AGTTCGAGTTATAGTTATCGTACAACCATTTTGGTTTGATTTCGAAAATGACGGAGCTGATGCCATCATT 3902
CPRB  3846 AGTTCGAGTTATAGTTATCGTACAACCACTTTGGCTTGATTTCGAAAATGACGGAGCTGATCCCATCATT 3915
           ***************************** ***** ************************* ********

CPRA  3903 CTCCTGGTTCCTCTCATAGTACAACTGGCACTTCTTCGAGAGGCTCAATTCCTCGTAGTTCCCGTCCAAG 3972
CPRB  3916 CTCCTGGTTCCTTTCATAGTACAACTGGCATTTCTTCGAGAGACTCAACTCCTCGTAGTTCCCGTCCAAG 3985
           ************ ***************** ********** ***** ***********************

CPRA  3973 ATATTCGGCAACAAGAGCCCGTACCGCTCACGGAGCATCAAGTCGTGGCCCTGGTTGTTCAACTTGTTGA 4042
CPRB  3986 ATATTCGGCAACAAGAGCCCGTAGCGCTCACGGAGCATCAAGTCGTGGCCCTGGTTGTTCAACTTGTTGA 4055
           ************************ ************************************************

CPRA  4043 TGAAGTCCGAGGTCAAGACAATCAACTGGATGTCGATGATCTGGTGCGGGAACAAGTTCTTGCATTTTAG 4112
CPRB  4056 TGAAGTCCGATGTCAAGACAATCAACTGGATGTCGATGATCTGGTGCGGAAACAAGTTCTTGCACTTTAG 4125
           ********** ****************************************** ************** *****

CPRA  4113 CTCGATGAAGTCGTACAACTCACACGTCGAGATATACTCCTGTTCCTCCTTCAAGAGCCGGATCCGCAAG 4182
CPRB  4126 CTCGATGAAGTCGTACAACT                                                  4145
           ********************

CPRA  4183 AGCTTGTGCTTCAAGTAGTCGTTG 4205
CPRB  4146                      4145
```

Figure 13D

```
CPRA    MALDKLDLYVIITLVVAVAAYFAKNQFLDQPQDTGFLNTDSGSNSRDVLLTLKGNNKNTL   60
CPRB    MALDKLDLYVIITLVVAVAAYFAKNQFLDQPQDTGFLNTDSGSNSRDVLLTLKGNNKNTL   60

CPRA    LLFGSQTGTAEDYANKLSRELHSRFGLKTMVADFADYDWDNFGDITEDILVFFIVATYGE   120
CPRB    LLFGSQTGTAEDYANKLSRELHSRFGLKTMVADFADYDWDNFGDITEDILVFFIVATYGE   120

                                  *
CPRA    GEPTDNADEFHTWLTEEADTLSTLKYTVFGLGNSTYEFFNAIGRKFDRLLSEKGGDRFAE   180
CPRB    GEPTDNADEFHTWLTEEADTLSTLRYTVFGLGNSTYEFFNAIGRKFDRLLSEKGGDRFAE   180

CPRA    YAEGDDGTGTLDEDFMAWKDNVFDALKNDLNFEEKELKYEPNVKLTERDDLSAADSQVSL   240
CPRB    YAEGDDGTGTLDEDFMAWKDNVFDALKNDLNFEEKELKYEPNVKLTERDDLSAADSQVSL   240

                                                  *
CPRA    GEPNKKYINSEGIDLTKGPFDHTHPYLARITETRELFSSKDRHCIHVEFDISESNLKYTT   300
CPRB    GEPNKKYINSEGIDLTKGPFDHTHPYLARITETRELFSSKERHCIHVEFDISESNLKYTT   300

CPRA    GDHLAIWPSNSDENIKQFAKCFGLEDKLDTVIELKALDSTYTIPFPTPITYGAVIRHHLE   360
CPRB    GDHLAIWPSNSDENIKQFAKCFGLEDKLDTVIELKALDSTYTIPFPTPITYGAVIRHHLE   360

                                      *           *              *
CPRA    ISGFVSRQFTLSLAGFAPDEETKKAFTRLGGDKQEFAAKVTRRKGNIADALLYSSNNAFH   420
CPRB    ISGFVSRQFTLSLAGFAPDEETKKTFTRLGGDKQEFATKVTRRKGNIADALLYSSNNTFH   420

                  **
CPRA    SDVPFEFLIENVPHLTPRYYSISSSSLSEKQLINVTAVVEAEEEADGRFVTGVVTNLLKN   480
CPRB    SDVPFEFLIENIQHLTPRYYSISSSSLSEKQLINVTAVVEAEEEADGRFVTGVVTNLLKN   480

        * *
CPRA    VEIVQNKTGEKPLVHYDLSGPRGKGNKGKLFVAVRRSNFKLPKNSTTFVILIGPGTGVAP   540
CPRB    IEIAQNKTGEKPLVHYDLSGPRGKGNKGKLFVAVRRSNFKLPKNSTTFVILIGPGTGVAP   540

CPRA    LRGFVRERVQQVKNGVNVGKTLLFYGCRNSNEDFLYKQEWAEYASVLGENFEMFNAFSRQ   600
CPRB    LRGFVRERVQQVKNGVNVGKTLLFYGCRNSNEDFLYKQEWAEYASVLGENFEMFNAFSRQ   600

CPRA    DPSKKVYVQDKILENSQLVHELLTEGAIIYVCGDASRMARDVQTTISKIVAKSREISEDK   660
CPRB    DPSKKVYVQDKILENSQLVHELLTEGAIIYVCGDASRMARDVQTTISKIVAKSREISEDK   660

CPRA    AAELVKSMKVQNRYQEDVW                                             680
CPRB    AAELVKSMKVQNRYQEDVW                                             680
```

Figure 14

C. tropicalis 20336 *CYP52* DNA Alignment of DS Sequence

```
CYP52A1A    1                                                                                                  0
CYP52A2A    1 GACCTGTGACGCTTCCGGTGTCTTGCCACCAGTCTCCAAGTTGACCGACGCCCAAGTCATGTACCACTTT                          70
CYP52A2B    1                                                                                                  0
CYP52A3A    1                                                                                GACATCATAAT      11
CYP52A3B    1                                                                                                  0
CYP52A5A    1                                                                                                  0
CYP52A5B    1                                                                                TTACAATCATGG      12
CYP52A8A    1                                                                                                  0
CYP52A8B    1                                                                                                  0
CYP52D4A    1                                                                                                  0

CYP52A1A    1                    CATATGCGCTAATCTTCTTTTTCTTTTTATCACAGGAGAAACTATCCCACCCCCACTTC                   59
CYP52A2A   71 ATTTCCGGTTACACTTCCAAGATGGCTGGTACTGAAGAAGGTGTCACGGAACCACAAGCTACTTTCTCCG                          140
CYP52A2B    1                                                                                                  0
CYP52A3A   12 GACCCGGTTATTTCGCCCTCAGGTTGCTTATTTGAGCCGTAAAGTGCAGTAGAAACTTTGCCTTGGGTTC                          81
CYP52A3B    1                                                                                                  0
CYP52A5A    1                                                                                TGGAGTC       7
CYP52A5B   13 AGCTCGCTAGGAACCCAGATGTCTGGGAGAAGCTCCGCGAAGAGGTCAACACGAACTTTGGCATGGAGTC                          82
CYP52A8A    1                                                                                                  0
CYP52A8B    1                                                                                                  0
CYP52D4A    1                                                                                                  0

CYP52A1A   60 GAAACACAATGACAACTCCTGCGTAACTTGCAAATTCTTGTCTGACTAATTGAAAACTCCGGACGAGTCA                          129
CYP52A2A  141 CTTGTTTCGGTCAACCATTCTTGGTGTTGCACCCAATGAAGTACGCTCAACAATTGTCTGACAAGATCTC                          210
CYP52A2B    1                                                GCTCAACAATTGTCTGACAAGATCTC                    26
CYP52A3A   82 AAACTCTAGTATAATGGTGATAACTGGTTGCACTCTTGCCATAGGCATGAAAATAGGCCGTTATAGTACT                          151
CYP52A3B    1                                                                                                  0
CYP52A5A    8 GCCAGACTTGCTCACTTTTGACTCCCTTCGAAACTCAAAGTACGTTCAGGCGGTGCTCAACGAAACGCTC                          77
CYP52A5B   83 GCCAGACTTGCTCACTTTTGACTCTCTTAGAAGCTCAAAGTACGTTCAGGCGGTGCTCAACGAAACGCTT                          152
CYP52A8A    1                                                                                                  0
CYP52A8B    1                                                AAAACCGATACAAGAAGAAGACAGTCAA                   28
CYP52D4A    1                                                                                                  0

CYP52A1A  130 GACCTCCAGTCAAACGGACAGACAGACAAACACTTGGTGCGATGTTCATACCTACAGACATGTCAACGGG                          199
CYP52A2A  211 GCAACACAAGGCTAACGCCTGGTTGTTGAACACCGGTTGGGTTGGTTCTTCTGCTGCTAGAGGTGGTAAG                          280
CYP52A2B   27 GCAACACAAGGCTAACGCCTGGTTGTTGAACACTGGTTGGGTTGGTTCTTCTGCTGCTAGAGGTGGTAAG                          96
CYP52A3A  152 ATATTTAATAAGCGTAGGAGTATAGGATGCATATGACCGGTTTTTCTATATTTTTAAGATAATCTCTAGT                          221
CYP52A3B    1                                                                CCTGCAGA                      8
CYP52A5A   78 CGTATCTACCCGGGGGTACCACGAAACATGAAGACAG--CTACGTGCAACACGACGTTGCCACGCGGAGG                          145
CYP52A5B  153 CGTATCTACCCGGGGGTGCCACGAAACATGAAGACAG--CTACGTGCAACACGACGTTGCCGCGTGGAGG                          220
CYP52A8A    1                                                                                                  0
CYP52A8B   29 CAAGAACGTTAATGTCAACCAGGCGCCAAGAAGACGG--TTTGGCGGACTTGGAAGAATGTGGCATTTGC                          96
CYP52D4A    1                                                                                                  0

CYP52A1A  200 TGTTAGACGACGGTTTCTTGCAAAGAC-AGGTGTTGGCATCTCGTACGATGGCAACTGCAGGAGGTGTCG                          268
CYP52A2A  281 AGATGCTCATTGAAGTACACCAGAGCCATTTTGGACGCTATCCACTCTGGTGAATTGTCCAAGGTTGAAT                          350
CYP52A2B   97 AGATGTTCATTGAAGTACACCAGAGCCATTTTGGACGCTATCCACTCTGGTGAATTGTCCAAGGTTGAAT                          166
CYP52A3A  222 AAATTTTGTATTCTCAGTAGGATTTCATCAAATTTCGCAACCAATTCTGGCGAAAAAATGATTCTTTTAC                          291
CYP52A3B    9 ATTCGCGGCCGCGTCGACAGAGTAGCAGTTATGCAAGCATGTGATTGTGGTTTTTGCAACCTGTTTGCAC                           78
CYP52A5A  146 AGGCA-AAGACGGCAAGGAACCTATCT-TGGTGCAGAAGGGACAGTCCGTTGGGTTGATTACTATTGCCA                          213
CYP52A5B  221 AGGCA-AAGACGGTAAGGAACCTATTT-TGGTGCAGAAGGGCCAGTCCGTTGGGTTGATTACTATTGCCA                          288
CYP52A8A    1                                                                                                  0
CYP52A8B   97 CCATG-ATGTTTATGTTCTGGAGAGGT-TTTTCAAGGAATCGTCATCCTCCGCCACCACAAGAACCACCA                          164
CYP52D4A    1                                                                                                  0
```

Figure 15A

```
CYP52A1A   269 ACTTCTCCTTTAGGCAATAGAAAAAGACTAAGAGAACAGCGTTTTTACAGGTTGCATTGGTTAATGTAGT  338
CYP52A2A   351 ACGAAACTTTCCCAGTCTTCAACTTGAATGTCCCAACCTCCTGTCCAGGTGTCCCAAGTGAAATCTTCAA  420
CYP52A2B   167 ACGAGACTTTCCCAGTCTTCAACTTGAATGTCCCAACCTCCTGCCCAGGTGTCCCAAGTGAAATCTTGCA  236
CYP52A3A   292 GTCAAAAGCTGA-ATAGTGCAGTTTAAAGCACCTAAAATCACATATACAGCCTCTAGATACGACAGAGAA  360
CYP52A3B    79 GACAAATGATCG-ACAGT-CGATT--ACGTAATCCATATTATTTAGAGGGGTAATAAAAAATAAAATGGCA  144
CYP52A5A   214 CGCAGACGGACCCAGAGTATTTTGGGGCCGACGCTGGTGAGTTTAAGCCGGAGAGATGGTTTGATTCA--  281
CYP52A5B   289 CGCAGACGGACCCAGAGTATTTTGGGGCAGATGCTGGTGAGTTCAAACCGGAGAGATGGTTTGATTCA--  356
CYP52A8A     1                                                                      0
CYP52A8B   165 GTTAACGAGATCCATATTCACAACCCACCGCAAGGTGACAATGCTCAACAACAACAGCAACAACAACA--  232
CYP52D4A     1                                                                      0

CYP52A1A   339 ATTTTTTTAGTCCCAGCATTCTGTGGGTTGCTCTGGGTTTCTAGAATAGGAAATCACAGGAGAATGCAAA  408
CYP52A2A   421 CCCAACCAAGGCCTGGACCGG-AAGGTGTTGACTCCTTCAACAAGGAAATCAAGTCTTTGGCTGGTAAGT  489
CYP52A2B   237 CCCAACCAAGGCCTGGACCG--AAGGTGTTGACTCCTTCAACAAGGAAATCAAGTCTTTGGCTGGTAAGT  304
CYP52A3A   361 GCTCTTTATGATCTGAAGAAGCATTAGAATAGCT---ACTATGAGCCACTATTGGTGTATATATTAGGGA  427
CYP52A3B   145 GCC----AGAATTTCAAACATTTTGCAAACAATGCAAAAGATGAGAAACTCCAACAGAAAAAATAAAAAA  210
CYP52A5A   282 AGCATGAAGAACTTGGGGTGTAAATACTTGCCGTTCAATGCTGGGCCACGGACTTGCTTGGGGCAGCAGT  351
CYP52A5B   357 AGCATGAAGAACTTGGGGTGTAAGTACTTGCCGTTCAATGCTGGGCCCCGGACTTGTTTGGGGCAGCAGT  426
CYP52A8A     1                                                                      0
CYP52A8B   293 ACCCCCACAAGAACAGTGGAATAATGCCAGTCAA-CAAAGAGTGGTGACAGACGAGGGAGAAAACGCAAG  361
CYP52D4A     1                                                                      0

CYP52A1A   409 TTCAGATGGAAGAACAAAGAGATAAAAAACAAAAAAAAACTGAGTTTTGCACCAATAGAATGTTTG----  474
CYP52A2A   490 TTGCTGAAAAC--TTCAAGACCTATGCTGACCAAGCTACCGCTGA--AGTGAGAGCTGCAGGTCCAGAAG  555
CYP52A2B   305 TTGCTGAAAAC--TTCAAGACCTATGCTGACCAAGCTACCGCTGA--AGTTAGAGCTGCAGGTCCAGAAG  370
CYP52A3A   428 TTGGTGCAATTAAGTACGTACTAATAAACAGAAGAAAATACTTAACCAATTTCTGGTGTATACTTAGTGG  497
CYP52A3B   211 ACTCCGCAGC--ACTCCGAACCAACAAAACAATGGGGGGCGCCAG--AATTATTGAC---TATT------  267
CYP52A5A   352 ACACTTTGATTGAAGCGAGCTACTTGCTAGTCCGGTTGGCCCAGACCTAC-CGGGCAATAGATTTG----  416
CYP52A5B   427 ACACTTTGATTGAAGCGAGCTATTTGCTAGTCAGGTTGGCGCAGACCTAC-CGGGTAATCGATTTG----  491
CYP52A8A     1                                                                      0
CYP52A8B   302 CAACAGTGGTTCTGATGCAAGATCAGCTACACCGCTTCATCAGGAAAAGC-AGGAGCTCCCACCAC----  366
CYP52D4A     1        GATGTGGTGCTTGATTTCTCGAGACACATCCTTGTGAGGTGCCATGAATCTGTACCTG----   58

CYP52A1A   475 -ATGATATCATCCACTCGCTAAACGAATCATGTGCGTGATCTTCTCTTTAGTTTTGGTCTATCATAAAAC  543
CYP52A2A   556 CTTAAAGATATTTATTCATTATTTAGTTTGCCTATTTATTTCTCATTACCCATC-ATCATTCAACACTAT  624
CYP52A2B   371 CTTAAAGATATTTATTCACTATTTAGTTTGCCTATTTATTTCTCATCACCCATC-ATCATTCAACAATAT  439
CYP52A3A   498 -TGAGCGACCTTTTCTGAACATTCGGGTCAAACTTTTTTTTGGAGTGCGACATCGATTTTTCGTTTGTGT  566
CYP52A3B   268 ----GTGACTTTTTTTTATTTTTTCCGTTAA--CTTTCATTGCAGTGAAGTGT--GTTACACGGGGTGGT  329
CYP52A5A   417 -CAGCCAGGATCGGCGTACC-CACCAAGAAAGAAGTCGTTGATCAACATGAGTGCTGCCGACGGGGTGTT  484
CYP52A5B   492 -CTGCCAGGGTCGGCGTACC-CACCAAGAAAGAAGTCGTTGATCAATATGAGTGCTGCCGATGGGGTGGT  559
CYP52A8A     1                                                                      0
CYP52A8B   357 -CATATGCCCATCACGAGCAACACCAGCAGGTTAGTGTATAGTAGTCTGTAGTTAAGTCAATGCAATGTA  435
CYP52D4A    59 -TCTGTAAGCACAGGGAACTGCTTCAACACCTTATTGCATATTCTGTCTATTGCAAGCGTGTGCTGCAAC  127

CYP52A1A   544 ACATGAAAGTGAAATCCAAA-TACACTACACTCCGGGTATTGTCCTTCGTTTTACAGATGTCTCATTGTC  612
CYP52A2A   625 ATATAAAGTTACTTCGGA----------TATCATTGTAATCGTGCGTGTCGCAATTGGATGATTTGGAA  683
CYP52A2B   440 ATATAAAGTTATTTCGGAAC-TCATA---TATCATTGTAATCGTGCGTGTTGCAATTGGGTAATTTGAAA  505
CYP52A3A   557 AATAATAGTGAACCTTTGTG-TAATAAATCTTCATGCAAGACTTGCATAATTCGAGCTTGGGAGTTCACG  635
CYP52A3B   330 GATGGTGTTGGTTTCTACAA-TGCAAGGGCACAGTTGAAGGTTTCCACATAACGT-TGCACCATATCAAC  397
CYP52A5A   465 TGT--AAAGCTTTATAAGGA-TGTAACGGTAGATGGATAGTTGTGTAGGAGGAGCGGAGATAAATTAGAT  551
CYP52A5B   560 TGT--AAAGTTTCACAAGGA-TCTAGATGGATATGTA-AGGTGTGTAGGAGGAGCGGAGATAAATTAGAT  625
CYP52A8A     1                                                                      0
CYP52A8B   436 CCA--ATAAGACTATCCCTT-CTTACAACCAAGTTTTCTGCCGCGCCTGTCTGGCA-ACAGATGCTGGCC  501
CYP52D4A   128 GATATCTGCCAAGGTATATAGCAGAACGTGCTGATGGTTCCTCCGGTCATATTCTGTTGGTAGTTCTGCA  197
```

Figure 15B

```
CYP52A1A   269 ACTTCTCCTTTAGGCAATAGAAAAAGACTAAGAGAACAGCGTTTTTACAGGTTGCATTGGTTAATGTAGT  338
CYP52A2A   351 ACGAAACTTTCCCAGTCTTCAACTTGAATGTCCCAACCTCCTGTCCAGGTGTCCCAAGTGAAATCTTGAA  420
CYP52A2B   167 ACGAGACTTTCCCAGTCTTCAACTTGAATGTCCCAACCTCCTGCCCAGGTGTCCCAAGTGAAATCTTGCA  236
CYP52A3A   292 GTCAAAAGCTGA-ATAGTGCAGTTTAAAGCACCTAAAATCACATATACAGCCTCTAGATACGACAGAGAA  360
CYP52A3B    79 GACAAATGATCG-ACAGT-CGATT--ACGTAATCCATATTATTTAGAGGGGTAATAAAAAATAAATGGCA  144
CYP52A5A   214 CGCAGACGGACCCAGAGTATTTTGGGGCCGACGCTGGTGAGTTTAAGCCGGAGAGATGGTTTGATTCA--  281
CYP52A5B   289 CGCAGACGGACCCAGAGTATTTTGGGGCAGATGCTGGTGAGTTCAAACCGGAGAGATGGTTTGATTCA--  356
CYP52A8A     1                                                                       0
CYP52A8B   165 GTTAACGAGATCCATATTCACAACCCACCGCAAGGTGACAATGCTCAACAACAACAGCAACAACAACA--  232
CYP52D4A     1                                                                       0

CYP52A1A   339 ATTTTTTTAGTCCCAGCATTCTGTGGGTTGCTCTGGGTTTCTAGAATAGGAAATCACAGGAGAATGCAAA  408
CYP52A2A   421 CCCAACCAAGGCCTGGACCGG-AAGGTGTTGACTCCTTCAACAAGGAAATCAAGTCTTTGGCTGGTAAGT  489
CYP52A2B   237 CCCAACCAAGGCCTGGACCG--AAGGTGTTGACTCCTTCAACAAGGAAATCAAGTCTTTGGCTGGTAAGT  304
CYP52A3A   361 GCTCTTTATGATCTGAAGAAGCATTAGAATAGCT---ACTATGAGCCACTATTGGTGTATATATTAGGGA  427
CYP52A3B   145 GCC----AGAATTTCAAACATTTTGCAAACAATGCAAAAGATGAGAAACTCCAACAGAAAAAATAAAAAA  210
CYP52A5A   282 AGCATGAAGAACTTGGGGTGTAAATACTTGCCGTTCAATGCTGGGCCACGGACTTGCTTGGGGCAGCAGT  351
CYP52A5B   357 AGCATGAAGAACTTGGGGTGTAAGTACTTGCCGTTCAATGCTGGGCCCCGGACTTGTTTGGGGCAGCAGT  426
CYP52A8A     1                                                                       0
CYP52A8B   233 ACCCCCACAAGAACAGTGGAATAATGCCAGTCAA-CAAAGAGTGGTGACAGACGAGGGAGAAAACGCAAG  301
CYP52D4A     1                                                                       0

CYP52A1A   409 TTCAGATGGAAGAACAAAGAGATAAAAAACAAAAAAAAACTGAGTTTTGCACCAATAGAATGTTTG----  474
CYP52A2A   490 TTGCTGAAAAC--TTCAAGACCTATGCTGACCAAGCTACCGCTGA--AGTGAGAGCTGCAGGTCCAGAAG  555
CYP52A2B   305 TTGCTGAAAAC--TTCAAGACCTATGCTGACCAAGCTACCGCTGA--AGTTAGAGCTGCAGGTCCAGAAG  370
CYP52A3A   428 TTGGTGCAATTAAGTACGTACTAATAAACAGAAGAAAATACTTAACCAATTTCTGGTGTATACTTAGTGG  497
CYP52A3B   211 ACTCCGCAGC--ACTCCGAACCAACAAAACAATGGGGGGCGCCAG--AATTATTGAC---TATT------  267
CYP52A5A   352 ACACTTTGATTGAAGCGAGCTACTTGCTAGTCCGGTTGGCCCAGACCTAC-CGGGCAATAGATTTG----  416
CYP52A5B   427 ACACTTTGATTGAAGCGAGCTATTTGCTAGTCAGGTTGGCGCAGACCTAC-CGGGTAATCGATTTG----  491
CYP52A8A     1                                                                       0
CYP52A8B   302 CAACAGTGGTTCTGATGCAAGATCAGCTACACCGCTTCATCAGGAAAAGC-AGGAGCTCCCACCAC----  366
CYP52D4A     1        GATGTGGTGCTTGATTTCTCGAGACACATCCTTGTGAGGTGCCATGAATCTGTACCTG----   58

CYP52A1A   475 -ATGATATCATCCACTCGCTAAACGAATCATGTGGGTGATCTTCTCTTTAGTTTTGGTCTATCATAAAAC  543
CYP52A2A   555 CTTAAAGATATTTATTCATTATTTAGTTTGCCTATTTATTTCTCATTACCCATC-ATCATTCAACACTAT  624
CYP52A2B   371 CTTAAAGATATTTATTCACTATTTAGTTTGCCTATTTATTTCTCATCACCCATC-ATCATTCAACAATAT  439
CYP52A3A   498 -TGAGGGACCTTTTCTGAACATTCGGGTCAAACTTTTTTTTGGAGTGCGACATCGATTTTTCGTTTGTGT  556
CYP52A3B   268 ----GTGACTTTTTTTTATTTTTTCCGTTAA--CTTTCATTGCAGTGAAGTGT--GTTACACGGGGTGGT  329
CYP52A5A   417 -CAGCCAGGATCGGCGTACC-CACCAAGAAAGAAGTCGTTGATCAACATGAGTGCTGCCGACGGGGTGTT  484
CYP52A5B   492 -CTGCCAGGGTCGGCGTACC-CACCAAGAAAGAAGTCGTTGATCAATATGAGTGCTGCCGATGGGGTGGT  559
CYP52A8A     1                                                                       0
CYP52A8B   357 -CATATGCCCATCACGAGCAACACCAGCAGGTTAGTGTATAGTAGTCTGTAGTTAAGTCAATGCAATGTA  435
CYP52D4A    59 -TCTGTAAGCACAGGGAACTGCTTCAACACCTTATTGCATATTCTGTCTATTGCAAGCGTGTGCTGCAAC  127

CYP52A1A   544 ACATGAAAGTGAAATCCAAA-TACACTACACTCCGGGTATTGTCCTTCGTTTTACAGATGTCTCATTGTC  612
CYP52A2A   625 ATATAAAGTTACTTCGGA----------TATCATTGTAATCGTGCGTGTCGCAATTGGATGATTTGGAA  683
CYP52A2B   440 ATATAAAGTTATTTCGGAAC-TCATA---TATCATTGTAATCGTGCGTGTTGCAATTGGGTAATTTGAAA  505
CYP52A3A   567 AATAATAGTGAACCTTTGTG-TAATAAATCTTCATGCAAGACTTGCATAATTCGAGCTTGGGAGTTCACG  635
CYP52A3B   330 GATGGTGTTGGTTTCTACAA-TGCAAGGGCACAGTTGAAGGTTTCCACATAACGT-TGCACCATATCAAC  397
CYP52A5A   485 TGT--AAAGCTTTATAAGGA-TGTAACGGTAGATGGATAGTTGTGTAGGAGGAGCGGAGATAAATTAGAT  551
CYP52A5B   550 TGT--AAAGTTTCACAAGGA-TCTAGATGGATATGTA-AGGTGTGTAGGAGGAGCGGAGATAAATTAGAT  625
CYP52A8A     1                                                                       0
CYP52A8B   436 CCA--ATAAGACTATCCCTT-CTTACAACCAAGTTTTCTGCCGCGCCTGTCTGGCA-ACAGATGCTGGCC  501
CYP52D4A   128 GATATCTGCCAAGGTATATAGCAGAACGTGCTGATGGTTCCTCCGGTCATATTCTGTTGGTAGTTCTGCA  197
```

Figure 15B

```
CYP52A1A   613 TTACTTTTGAGGTCATAGGAGTTGCCTGTGAGAGATCACAGAGATTATCACACTCACATTTATCGTAGTT  682
CYP52A2A   684 CTGCGCTTGAAACGGATTCATGCACGAAGCGGAGA-TAAAAGATTACGT---AATTTATCTCCTGATACA  749
CYP52A2B   506 CTGTAGTTGGAACGGATTCATGCACGATGCGGAGA-TAACACG---------AGATTATCTCCTAAGACA  565
CYP52A3A   636 C--CAATTTGACCTCGTTCATGTGATAAAAGAAAAGCCAAAAGGTAATT---AGCAGACGC---AATGGG  697
CYP52A3B   398 T--CAATTTATCCTCATTCATGTGATAAAAGAAGAGCCAAAAGGTAATT---GGCAGACCCCCCAAGGGG  462
CYP52A5A   552 TTGATTTTG---TGTAAGGTTTTGGATGTCAACCTACTCCGCACTTCATGCA-GTGTGTGTGACACAAGG  617
CYP52A5B   626 TTGATTTTG---TGTAAGGTTTAGCACGTCAAGCTACTCCGCACTTTGT----GTGTAGGGAGCACA---  685
CYP52A8A     1                                                                      0
CYP52A8B   502 GACACACTT---TCAACTGAGTTTGGTCTAGAATTCTTGCACATGCACGACA-AGGAAACTCTTACAAAG  567
CYP52D4A   198 GGTAAATTTGGATGTCAGGTAGTGGAGGGAGGTTTGTATCGGTTGTGTT-TTCTTCTTCCTCTCTCTCTG  266

CYP52A1A   683 TCCTATCTCATGCTGTGTGTCTCTGGTTGGTTCATGAGTTTGGATT--GTTGTACATTAAAGGAATCGCT  750
CYP52A2A   750 ATTTTAGCCGTGTTCACACGCCCTTCTTTGTT-CTGAGCGAAGGAT--AAATAATTAGACTTCCACAGCT  816
CYP52A2B   566 ATTTTGGCCTCATTCACACGCCCTTCTT-----CTGAGCTAAGGAT--AAATAATTAGACTTCACAAGTT  628
CYP52A3A   698 AACATGGAGTGGAAAGCAATGGAAGCACGCCC-AGGACGGAGTAATTTAGTCCACACTACATCTGGGGGT  766
CYP52A3B   463 AACACGGAGTAGAAAGCAATGGAAACACGCCC-ATGACAGTGCCATTTAGCCCACAACACATCTAGTATT  531
CYP52A5A   618 GTGTACTACGTGTGCGTGTGCGCCAAGAGACA---GCCCAAGGGGG--TGGTAGTGT-GTGTTGGCGGAA  681
CYP52A5B   686 ---TACTCCGTCTGCGCCTGTGCCAAGAGACG---GCCCAGGGG-------TAGTGT-GTGGTGGTGGAA  741
CYP52A8A     1    GAATTCTTTGGATCTAATTCCAGCTGATC---TTGCTAATCCT--TATCAACGTAGTTGTGATCATT   62
CYP52A8B   568 --ACAACACTTGTGCTCTGATGCCACTTGATC---TTGCTAAGCCT--TATCAACGTAATTGAGATCATT  630
CYP52D4A   267 ATTCAACCTCCACGTCTCCTTCGGGTTCTGTGTCTGTGTCTGAGTC--GTACTGTTGGATTAAGTCCATC  334

CYP52A1A   751 GGAAAGCAAAGCTAACTAAATTTTCTTTGTCACAGGTACACTAACCTGTAAAACTTCACTGCCACGCCAG  820
CYP52A2A   817 CATTCTAATTTCCGT---CACGCGAATATTGAA------------GGGGGGTACATGTGGCCGCTGAA-  869
CYP52A2B   629 CATTAAAATATCCGT---CACGCGAAAACTGCAACAATAAGGAAGGGGGGGGTAGACGTAGCCGATGAA-  694
CYP52A3A   767 ----TTTTTTTTTGTGCGCAAGTACACACCTGGACT-TTAGTTTTTGCCCCATAAAGTTAACAATCTAA-  830
CYP52A3B   532 CTTTTTTTTTTTTGTGCGCAGGTGCACACCTGGACT-TTAGTTATTGCCCCATAAAGTTAACAATCTCA-  599
CYP52A5A   682 GTGCATGTGACACA---ACGCGTGGGTTCTGGCCAATGGTGGACTAAGTGCAGGTAAGCAGCGACCTGAA  748
CYP52A5B   742 GTGCATGTGACACA---ATACCCTGGTTCTGGCCAATTGGGGATTTAGTGTAGGTAAGCTGCGACCTGAA  808
CYP52A8A    63 GTTTGTCTGAATTAT--ACACACCAGTGGAAGAATATGGTCTAATTTGCACGTCCCACTGGCATTGTG--  128
CYP52A8B   631 GTTTGTCTGAATTAT--ACACACCAGTGGAAGAATCTGGTCTAATCTGCACGCCTCATGGGCATTGTG--  696
CYP52D4A   335 GCATGTGTGAAAAAAAGTAGCGCTTATTTAGACAACCAGTTCGTTGGGCGGGTATCAGAAATAGTCTGTT  404

CYP52A1A   821 TCTTTCCTGATTGGGCAAGTGCACAAACTACA-ACCTGCAAAACAG----CACTCCGCTTGTCACAGGTT  885
CYP52A2A   870 -TGTGGGGG--CAGTAAACGCAGTCTCTC----------------CTCTCCCAGGAATAGTGCAACGG  918
CYP52A2B   695 -TGTGGGGTGCCAGTAAACGCAGTCTCTCTCTCCCCCCCCCCCCCCCCCCCTCAGGAATAGTACAACGG  763
CYP52A3A   831 -CCTTTGGC-TCTCCAACTCTCTCCGCCCCCAAATATTCGTTTTT-ACACCCTCAAGCTAGCGACAGCAC  897
CYP52A3B   600 -CCTTTGGC-TCTCCCAGTGTCTCCGCCTCCAGATGCTCGTTTT--ACACCCTCGAGCTAACGACAACAC  665
CYP52A5A   749 ACATTCCTCAACGCTTAAGACACTGGTGG-TAGAGATGCGGACCAGG-----CTATTCTTGTCGT-GCTA  811
CYP52A5B   809 ACACTCCTCAACGCTTGAGACACTGGTGGGTAGAGATGCGGGCCAGGA--GGCTATTCTTGTCGT-GCTA  875
CYP52A8A   129 -TGTTT-----GTGGGGGGGGGGGGGTGCACACATTTTTAGTGCCA----TTCTTTGTTGATTAC-CCCT  187
CYP52A8B   697 -TGTTTT--GGGGGGGGGGGGGGGGTGCACACATTTTTAGTGCGAATGTTTGTTTGCTGGTTCC-CCCT  762
CYP52D4A   405 GTGCACGACCATGAGTATGCAACTTGACGAGACGTCGTTAGGA-----ATCCACAGAATGATAGCAGGAA  469

CYP52A1A   886 GTCTCCTCTCAACCAACAAAAAAATAAGATTAAACTTTCTTTGCTCATGCATCAATCGGAGTTATCTCTG  955
CYP52A2A   919 AGGAAGGATAACGGATAGAAAGCGGAATGCGAGGAAAAT--TTTGAACGCGCAAGAAAAGCAATATCCGG  986
CYP52A2B   764 GGGAAGGATAACGGATAGCAAGTGGAATGCGAGGAAAAT--TTTGAATGCGCAAGGAAAGCAATATCCGG  831
CYP52A3A   898 AACACCCATTAGAGGAATGGGGCAAAGTTAAACACTTTTGGCTTCAATGATTCCTATTCGCTACTACATT  967
CYP52A3B   666 AACACCCATGAGGGGAATGGG-CAAAGTTAAACACTTTTGGTTTCAATGATTCCTATTTGCTACT-----  729
CYP52A5A   812 CCCGGCGCATGGA-AAATCAACTGCGGGAAGAA--TAAATTTATCCGTAGAATCCACAGAGCG------G  872
CYP52A5B   876 CCCG-TGCACGGA-AAATCGATTGAGGGAAGAA--CAAATTTATCCGTGAAATCCACAGAGCG------G  935
CYP52A8A   188 CCCCCCTATCAT---TCATTCCCACAGGATTAG--TTTTTTCCTCACTGGAATTCGCTGTCC--------  244
CYP52A8B   763 CCCCCCTCCCCCCTATCATGCCCACAGGATTAG--TTTTTTCCTCACTGGAATTCGCTGTCC--------  822
CYP52D4A   470 GCTTACTACGTGAGAGATTCTGCTTAGAGGATG--TTCTCTTCTTGTTGATTCCATTAGGTGGGTATCAT  537
```

Figure 15C

```
CYP52A1A   956 A--AAGAGTTGCCTTTGTGTAATGTGTGCCAAA-CTCAAACTGCAAAACTAACCACAGAATGAT------ 1016
CYP52A2A   987 GCTACCAGGTTTTGAGCCAGGGAACACACTCCTATTTCTGCTCAATGACTGAACATAGAAAAAA-- --- 1050
CYP52A2B   832 GCTATCAGGTTTTGAGCCAGGGGACACACTCCT-CTTCTGCACAAAAACTTAACGTAGACAAAAAAAAAA 900
CYP52A3A   968 CTTCTCTTGTTTTGTGCTTTGAATTGCACCATGTGAAATAAACGACAATTATATATACCTTTTCATC--- 1034
CYP52A3B   730 ---CTCTTGTTTTGTGTTTTGATTTGCACCATGTGAAATAAACGACAATTATATATACCTTTTCGTC--- 793
CYP52A5A   873 A--TAAATTTGCCCACCTCCATCATCAACCACG-CCGCCACTAACTACATCACTCCCCTATTTT------ 933
CYP52A5B   936 A--TAAATTTGTCACATTGCTGCGTTGCCCAC-----------CCACAGCATTCTC------------ 978
CYP52A8A   245 ------ACCTGTCAACCCCCCCCCCCCCCCCC-CCACTGCC--CTACCCTGCCCTGC---------- 293
CYP52A8B   823 ------ACCTGTCAACCCCCTCAC-------------------TGCCCTGCCCTGC---------- 853
CYP52D6A   538 CTCCGGTGGTGACAACTTGACACAAGCAGTTCCGAGAACCACCCACAACAATCACCATTCCAGC------ 601

CYP52A1A  1017 TTCCCTCACAATTATATAAACTCACCCACATTTCCACAGACCGTAATTTCATGTCTCAC-TTTCTCTTTT 1085
CYP52A2A  1051 -----CACCAAGACGCAATGAAACGCACATGGACATTTAGACCTCCCCACATGTGATAGTTTGTCTTAAC 1115
CYP52A2B   901 AACTCCACCAAGACACAATGAATCGCACATGGACATTTAGACCTCCCCACATGTGAAAGCTTCTCTGGCG 970
CYP52A3A  1035 CCTCCTCCTATATCTCTTTTTGCTAC-ATTTTGTTTTTTACGTTTCTTGCTTTTGCACTCTCCCACTCCC 1103
CYP52A3B   794 TGTCCTCCAATGTCTCTTTTTGCTGCCATTTTGCTTTTTGCTTTTTGCTTTTGCACTCTCTCCCACTCCC 863
CYP52A5A   934 CTCTCTCTCTCTTTGTCTTACTCCGCTCCCGTTTCCTTAGCCACAGATACACACCCACT-GCAAACAGCA 1002
CYP52A5B   979 TTTTCTCTCTCTTTGTCTTACTCCGCTCCTGTTTCCTTATCCAGAAATACACACCAACTCATATAAAGAT 1048
CYP52A8A   294 CCTGCACGTCCTGTGTTTTGTGCTGTGTCTTTCCCACGCTATAAAAGCCCTGGCGTCCGGCCAAGGTTTT 363
CYP52A8B   854 CCTGCACGCCCTGTGTTTTGTGCTGTGGCACTCCCACGCTATAAAAGCCCTGGCGTACGGCCAAGGTTTT 923
CYP52D6A   602 TATCACTTCTACATGTCAACCTACGATGTATCTCATCACCATCTAGTTTCTTGGCAATCGTTTATTTGTT 671

CYP52A1A  1086 GCTCTTCTTTTACTTAGTCAGGTTTGATAACTTCCTTTTTTATTACCCTATCTTATTTATTTATTTATTC 1155
CYP52A2A  1116 AGA------AAAGTATAATAAGAACCCATGCCGTCCCTTTTCTTTCGCCGCTTCAACTTTTTTTTTTTTA 1179
CYP52A2B   971 AAAGCAAAAAAAGTATAATAAGGACCCATGCCTTCCCTCTTCCTGGGCCGTTTCAACTTTTTCTTTTTCT 1040
CYP52A3A  1104 ACAA--------------------------AGAAAAAAAAAACTACACTATGTCGTCTTCTCCATCGTTT 1146
CYP52A3B   864 ACAATCAGTGCAGCAACACACAAAGAAGAAAAATAAAAAAACCTACACTATGTCGTCTTCTCCATCGTTT 933
CYP52A5A  1003 GCA--ACAATTATAAAGATACGCC-----AGGCCCACCTTCTTTCTTTTCTTCACTTTTTTGACTGC-A 1064
CYP52A5B  1049 ACG--CTAGCCCAGCTGTCTTTCT-----TTTCTTCACTTTTTTTGGTGTGTTGCTTTTTTGGCTGC-T 1110
CYP52A8A   364 TCCACCCAGCCAAAAAAACAGTCTAAAAAATTTGGTTGATCCTTTTGGTTGCAAGGTTTT---CCAC-C 429
CYP52A8B   924 TCCTCACAGCCAAAAAAA----------AATTTGGCTGATCCTTTTGGGCTGCAAGGTTTTTCACCAC-C 982
CYP52D6A   672 ATGGGTCAACATCCAATACAACTCCACCAA--TGAAGAAGAAAAACGGAAAGCAGAATACCAGAATGACA 739

CYP52A1A  1156 ATTTATACCAACCAACC--AACCATGGCCACACAAGAAATCATCGATTCTGTACTTCCGTACTTGACCAA 1223
CYP52A2A  1180 TCTT-----------ACACACATCACGACCA-TGACTGTACACGATATTATCGCCACATACTTCACCAA 1236
CYP52A2B  1041 TTGTCTATCAACACACACACCTCACGACCA-TGACTGCACAGGATATTATCGCCACATACATCACCAA 1109
CYP52A3A  1147 GCCC-------AAGAGGTTCTCGCTACCACTAGTCCTTACATCGAGTACTTTCTTGACA-ACTACACCAG 1208
CYP52A3B   934 GCTC-------AGGAGGTTCTCGCTACCACTAGTCCTTACATCGAGTACTTTCTTGACA-ACTACACCAG 995
CYP52A5A  1065 ACTTTCTACAATCCACCACAGCCACCACCACAGCCGCTATGATTGAACAACTCCTAGAATATT------- 1127
CYP52A5B  1111 ACTTTCTACAACC-------ACCACCACCACCACCACCATGATTGAACAAATCCTAGAATATT------- 1165
CYP52A8A   430 ACCACTTCCACCA--CCTCAACTATTCGAACAA--AAGATGCTCGATCAGATCTTACATTACT------- 488
CYP52A8B   983 ACCACCACCACCA--CCTCAACTATTCAAACAA--AGGATGCTCGACCAGATCTTCCATTACT------- 1041
CYP52D6A   740 GTGTG----AGTTCCTGACCATTGCTAATCTA-TGGCTATATCTAGTTTGCTATCGTGGGATG------- 797

CYP52A1A  1224 ATGGTACACTGTGATTACTGCAGCAGTATTAGTCTTCCTTATCTCCACAAACATCAAGAACTACGTCAAG 1293
CYP52A2A  1237 ATGGTACGTGATAGTACCACTCGCTTTGATTGCTTATAGAGTCCTCGACTACTTCTATGGCAGATACTTG 1306
CYP52A2B  1110 ATGGTACGTGATAGTACCACTCGCTTTGATTGCTTATAGGGTCCTCGACTACTTTTACGGCAGATACTTG 1179
CYP52A3A  1209 ATGGTACTACTTCATACCTTTGGTGCTTCTTTCGTTGAACTTTATAAGTTTGCTCCACACAAGGTACTTG 1278
CYP52A3B   996 ATGGTACTACTTCATCCCTTTGGTGCTTCTTTCGTTGAACTTCATCAGCTTGCTCCACACAAAGTACTTG 1065
CYP52A5A  1128 --GGTATGTCGTTGTGCCAGTGTTGTACATCATCAAACAACTCCTTGCATACACAAAGACTCGCGTCTTG 1195
CYP52A5B  1167 --GGTATATTGTTGTGCCTGTGTTGTACATCATCAAACAACTCATTGCCTACAGCAAGACTCGCGTCTTG 1234
CYP52A8A   489 --GGTACATTGTCTTGCCATTGTTGGCCATTATCAACCAGATCGTGGCTCATGTCAGGACCAATTATTTG 556
CYP52A8B  1042 --GGTACATTGTCTTGCCATTGTTGGTCATTATCAAGCAGATCGTGGCTCATGCCAGGACCAATTATTTG 1109
CYP52D6A   798 -TGATCTGTGTCGTCTTCATTTGCGTTTGTGTTTATTTCGGGTAT-GAATATTGTTATACTAAATACTTG 865
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Figure 15D

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CYP52A1A  1628 TGTTGAGACCACAGTTTGCTAGAGACCAGATTGGACACGTTAAAGCCTTGGAACCACACATCCAAATCAT 1697
CYP52A2A  1647 TGTTGAGACCACAGTTTGCCAGAGAACAGATTTCCCACGTCAAGTTGTTGGAGCCACACGTTCAGGTGTT 1716
CYP52A2B  1520 TGTTGAGACCACAGTTTGCCAGAGAACAGATTTCCCACGTCAAGTTGTTGGAGCCACACATGCAGGTGTT 1589
CYP52A3A  1628 TGTTGAGACCACAGTTTGCTAGAGAACAGGTTTCTCACGTCAAGTTGTTGGAGCCACACGTTCAGGTGTT 1697
CYP52A3B  1415 TGTTGAGACCACAGTTTGCTAGAGAACAGGTTTCCCACGTCAAGTTGTTGGAACCACACGTTCAGGTGTT 1484
CYP52A5A  1536 TGTTGAGACCACAGTTTGCCAGAGAACAAGTTGCTCATGTGACGTCGTTGGAACCACACTTCCAGTTGTT 1605
CYP52A5B  1575 TGTTAAGACCACAGTTTGCCAGAGAACAAGTTGCTCATGTGACGTCGTTGGAACCACACTTCCAGTTGTT 1644
CYP52A8A   885 TGTTGAGACCACAGTTTGCCAGAGAACAAGTTGCTCATGTGACGTCGTTGGAACCACACTTCCAGTTGTT  954
CYP52A8B  1438 TGTTGAGACCACAGTTTGCCAGAGAGCAAGTTGCTCATGTGACGTCGTTGGAACCACATTTCCAGTTGTT 1507
CYP52D4A  1206 TGTTGCGTCCGCAATTTGCCAAAGATCGGGTTTCTCATATCCTGGATCTAGAACCGCATTTTGTGTTGCT 1275
               ****  * ** ** ***** * *** *   **   **  *       * ** ** **  *    *  *

CYP52A1A  1698 GGCTAAGCAGATCAAGTTGAACCAGGGAAAGACTTTCGATATCCAAGAATTGTTCTTTAGATTTACCGTC 1767
CYP52A2A  1717 CTTCAAACACGTCAGAAAGGCACAGGGCAAGACTTTTGACATCCAGGAATTGTTTTTCAGATTGACCGTC 1786
CYP52A2B  1590 CTTCAAGCACGTCAGAAAGGCACAGGGCAAGACTTTTGACATCCAAGAATTGTTTTTCAGATTGACCGTC 1659
CYP52A3A  1698 CTTCAAGCACGTTAGAAAGCACCGCGGTCAAACGTTCGACATCCAAGAATTGTTCTTCAGGTTGACCGTC 1767
CYP52A3B  1485 CTTCAAGCACGTTAGAAAACACCGCGGTCAGACTTTTGACATCCAAGAATTGTTCTTCAGATTGACCGTC 1554
CYP52A5A  1606 GAAGAAGCATATTCTTAAGCACAAGGGTGAATACTTTGATATCCAGGAATTGTTCTTTAGATTTACCGTT 1675
CYP52A5B  1645 GAAGAAGCATATCCTTAAACACAAGGGTGAGTACTTTGATATCCAGGAATTGTTCTTTAGATTTACTGTC 1714
CYP52A8A   955 GAAGAAGCATATCCTTAAACACAAGGGTGAGTACTTTGATATCCAGGAATTGTTCTTTAGATTTACCGTT 1577
CYP52A8B  1508 GAAGAAGCATATTCTTAAGCACAAGGGTGAATACTTTGATATCCAGGAATTGTTCTTTAGATTTACCGTT 1577
CYP52D4A  1276 TCGGAAGCACATTGATGGCCACAATGGAGACTACTTCGACATCCAGGAGCTCTACTTCCGGTTCTCGATG 1345
                  ** **  *           **  *   ** ** ***** **  * *  **  * **  *  *

CYP52A1A  1768 GACACCGCTACTGAGTTCTTGTTTGGTGAATCCGTTCACTCCTTGTACGATGAAAAATTGGGCATCCCAA 1837
CYP52A2A  1787 GACTCCGCCACCGAGTTTTTGTTTGGTGAATCCGTTGAGTCCTTGAGAGATGAATCTATCGGCATGTCCA 1856
CYP52A2B  1560 GACTCCGCCACTGAGTTTTTGTTTGGTGAATCCGTTGAGTCCTTGAGAGATGAATCTATTGGGATGTCCA 1729
CYP52A3A  1768 GACTCCGCCACCGAGTTCTTGTTTGGTGAGTCTGCTGAATCCTTGAGGGACGAATCTATTGGATTGACCC 1837
CYP52A3B  1555 GACTCCGCCACCGAGTTCTTGTTTGGTGAGTCTGCTGAATCCTTGAGAGACGACTCTGTTGGTTTGACCC 1624
CYP52A5A  1676 GATTCGGCCACGGAGTTCTTATTTGGTGAGTCCGTGCACTCCTTAAAGGACGAATCTATTGGTATCAACC 1745
CYP52A5B  1715 GACTCGGCCACGGAGTTCTTATTTGGTGAGTCCGTGCACTCCTTAAAGGACGAAACTATCGGTATCAACC 1784
CYP52A8A  1025 GACTCGGCCACGGAGTTCTTATTTGGTGAGTCCGTGCACTCCTTAAGGGACGAGGAAATTGGCTACGACA 1094
CYP52A8B  1578 GATTCAGCGACGGAGTTCTTATTTGGTGAGTCCGTGCACTCCTTAAGGGACGAGGAAATTGGCTACGATA 1647
CYP52D4A  1346 GATGTGGCGACGGGGTTTTTGTTTGGCGAGTCTGTGGGGTCGTTGAAAGACGAAGATGCGAGG------- 1408
               **  .  ** ** * *** ** ***** ** ** *    ** **   ** **         *

CYP52A1A  1838 CTCCAAACGAAA---TCCCAGGAAGAGAAAACTTTGCCGCTGCTTTCAACGTTTCCCAACACTACTTGGC 1904
CYP52A2A  1857 TCAATGCGCTTGACTTTGACGGCAAGGCTGGCTTTGCTGATGCTTTTAACTATTCGCAGAATTATTTGGC 1926
CYP52A2B  1730 TCAATGCACTTGACTTTGACGGCAAGGCTGGCTTTGCTGATGCTTTTAACTACTCGCAGAACTATTTGGC 1799
CYP52A3A  1838 CAACCACCAAGGATTTCGATGGCAGAAGAGATTTCGCTGACGCTTTCAACTATTCGCAGACTTACCAGGC 1907
CYP52A3B  1625 CAACCACCAAGGATTTCGAAGGCAGAGGAGATTTCGCTGACGCTTTCAACTACTCGCAGACTTACCAGGC 1694
CYP52A5A  1746 AAGACGATATAGATTTTGCTGGTAGAAAGGACTTTGCTGAGTCGTTCAACAAAGCCCAGGAATACTTGGC 1815
CYP52A5B  1785 AAGACGATATAGATTTTGCTGGTAGAAAGGACTTTGCTGAGTCGTTCAACAAAGCCCAGGAGTATTTGTC 1854
CYP52A8A  1095 CGAAAGACATGT---CTGAAGAAAGACGCAGATTTGCCGACGCGTTCAACAAGTCGCAAGTCTACGTGGC 1151
CYP52A8B  1648 CGAAGGACATGG---CTGAAGAAAGACGCAAATTTGCCGACGCGTTCAACAAGTCGCAAGTCTATTTGTC 1714
CYP52D4A  1409 ------------------------------TTCCTGGAAGCATTCAATGAGTCGCAGAAGTATTTGGC 1446
                                             **   *  * ** **    * **   **   * *

CYP52A1A  1905 CACCAGAAGTTACTCCCAGACTTTTTACTTTTTGACCAACCCTAAGGAATTCAGAGACTGTAACGCCAAG 1974
CYP52A2A  1927 TTCGAGAGCGGTTATGCAACAATTGTACTGGGTGTTGAACGGGAAAAAGTTTAAGGAGTGCAACGCTAAA 1996
CYP52A2B  1800 TTCGAGAGCGGTTATGCAACAATTGTACTGGGTGTTGAACGGGAAAAAGTTTAAGGAGTCGATTGCTGTC 1977
CYP52A3A  1908 CTACAGATTTTTGTTGCAACAAATGTACTGGATCTTGAATGGCTCGGAATTCAGAAAGTCGATTGCTGTC 1977
CYP52A3B  1695 CTACAGATTTTTGTTGCAACAAATGTACTGGATTTTGAATGGCGCGGAATTCAGAAAGTCGATTGCCATC 1764
CYP52A5A  1816 TATTAGAACCTTGGTGCAGACGTTCTACTGGTTGGTCAACAACAAGGAGTTTAGAGACTGTACCAAGCTG 1885
CYP52A5B  1855 TATTAGAATTTTGGTGCAGACCTTCTACTGGTTGATCAACAACAAGGAGTTTAGAGACTGTACCAAGCTG 1924
CYP52A8A  1162 CACCAGAGTTGCTTTACAGAACTTGTACTGGTTGGTCAACAACAAAGAGTTCAAGGAGTGCAATGACATT 1231
CYP52A8B  1715 CACCAGAGTTGCTTTACAGACATTGTACTGGTTGGTCAACAACAAAGAGTTCAAGGAGTGCAACGACATT 1784
CYP52D4A  1447 AACTAGGGCAACGTTGCACGAGTTGTACTTTCTTTGTGACGGGTTTAGGTTTCGCCAGTACAACAAGGTT 1516
                  **          **    * ***  *  *    *          **    * *  *
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Figure 15F

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CYP52A1A  1975 GTCCACCACTTGGCCAAGTACTTTGTCAACAAGGCCTTGAACTTTACTCCTGAAGAACTCGAAGAGAAAT 2044
CYP52A2A  1997 GTGCACAAGTTTGCTGACTACTACGTCAACAAGGCTTTGGACTTGACGCCTGAACAATTGGAAAAGCAGG 2066
CYP52A2B  1870 GTGCACAAGTTTGCTGACTATTACGTCAGCAAGGCTTTGGACTTGACACCTGAACAATTGGAAAAGCAGG 1939
CYP52A3A  1978 GTGCACAAGTTTGCTGACCACTATGTGCAAAAGGCTTTGGAGTTGACCGACGATGACTTGCAGAAACAAG 2047
CYP52A3B  1765 GTGCACAAGTTTGCTGACCACTATGTGCAAAAGGCTTTGGAGTTGACCGACGATGACTTGCAGAAACAAG 1834
CYP52A5A  1886 GTGCACAAGTTCACCAACTACTATGTTCAGAAAGCTTTGGATGCTAGCCCAGAAGAGCTTGAAAAGCAAA 1955
CYP52A5B  1925 GTGCACAAGTTTACCAACTACTATGTTCAGAAAGCTTTGGATGCTACCCCAGAGGAACTTGAAAAGCAAG 1994
CYP52A8A  1232 GTCCACAAGTTTACCAACTACTATGTTCAGAAAGCCTTGGATGCTACCCCAGAGGAACTTGAAAAACAAG 1854
CYP52A8B  1785 GTCCACAAGTTCACCAACTACTATGTTCAGAAAGCCTTGGATGCTACCCCAGAGGAACTTGAAAAACAAG 1854
CYP52D4A  1517 GTGCGAAAGTTCTGCAGCCAGTGTGTCCACAAGGCGTTACATGTTGCACCGGAAGACACC---------A 1577
               ** *  * **       * *  **   ** ** ** *        **  *

CYP52A1A  2045 CCAAGTCCGGTTACGTTTTCTTGTACGAATTGGTTAAGCAAACCAGAGATCCAAAGGTCTTGCAAGATCA 2114
CYP52A2A  2067 ATGGTT------ATGTGTTTTTGTACGAATTGGTCAAGCAAACCAGAGACAAGCAAGTGTTGAGAGACCA 2130
CYP52A2B  1940 ATGGTT------ATGTGTTCTTGTACGAGTTGGTCAAGCAAACCAGAGACAGGCAAGTGTTGAGAGACCA 2111
CYP52A3A  2048 ACGGCT------ATGTGTTCTTGTACGAGTTGGCTAAGCAAACCAGAGACCCAAAGGTCTTGAGAGACCA 1898
CYP52A3B  1835 ACGGCT------ATGTGTTCTTGTACGAGCTTGTCAAGCAGACAAGAGACCCCAATGTGTTGCGTGACCA 2019
CYP52A5A  1956 GTGGGT------ATGTGTTCTTGTATGAGCTTGTCAAGCAGACGAGAGACCCCAAGGTGTTGCGTGACCA 2058
CYP52A5B  1995 GCGGGT------ATGTGTTCTTGTATGAGCTTGTCAAGCAGACGAGAGACCCCAAGGTGTTGCGTGACCA 1365
CYP52A8A  1302 GCGGGT------ATGTGTTCTTGTATGAGCTTGTCAAGCAGACGAGAGACCCCAATGTGTTGCGTGACCA 1918
CYP52A9B  1855 GCGGGT------ATGTGTTCTTGTACGAGCTTGCCAAGCAGACGAAAGACCCCAATGTGTTGCGTGACCA 1641
CYP52D4A  1578 GCGAGT------ACGTGTTTCTCCGCGAGTTGGTCAAACACACTCGAGATCCCGTTGTTTTACAAGACCA 1641
                     *      * ** **  *    **  * *  ** ** **  ***      ** **    ** **

CYP52A1A  2115 ATTGTTGAACATTATGGTTGCCGGAAGAGACACCACTGCCGGTTTGTTGTCCTTTGCTTTGTTTGAATTG 2184
CYP52A2A  2131 ATTGTTGAACATCATGGTTGCTGGTAGAGACACCACCGCCGGTTTGTTGTCGTTTGTTTTCTTTGAATTG 2200
CYP52A2B  2004 GTTGTTGAACATCATGGTTGCCGGTAGAGACACCACCGCCGGTTTGTTGTCGTTTGTTTTCTTTGAATTG 2073
CYP52A3A  2112 GTTATTGAACATTTTGGTTGCCGGTAGAGACACGACCGCCGGTTTGTTGTCATTTGTTTTCTACGAGTTG 2181
CYP52A3B  1899 GTTGTTGAACATTTTGGTTGCCGGTAGAGACACGACCGCCGGTTTGTTGTCGTTTGTGTTCTACGAGTTG 1968
CYP52A5A  2020 GTCTTTGAACATCTTGTTGGCCGGAAGAGACACCACTGCTGGGTTGTTGTCGTTTGCTGTCTTTGAGTTG 2089
CYP52A5B  2059 GTCTTTGAACATCTTGTTGGCAGGAAGAGACACCACTGCTGGGTTGTTGTCCTTTGCTGTGTTTGAGTTG 2128
CYP52A8A  1366 GTCTTTGAACATCTTGTTGGCAGGAAGAGACACCACTGCTGGGTTGTTGTCCTTTGCTGTGTTTGAGTTG 1435
CYP52A8B  1919 GTCTTTGAACATCTTGTTGGCTGGAAGGGACACCACTGCTGGGTTGTTGTCCTTTGCTGTGTTTGAGCTA 1988
CYP52D4A  1642 AGCGTTGAACGTCTTGCTTGCTGGACGCGACACCACCGCGTCGTTATTATCGTTTGCAACATTTGAGCTA 1711
                  ******* *  ** * ** **  * ***** ** **    ** ** ** ****     *  **  *

CYP52A1A  2185 GCTAGACACCCAGAGATGTGGTCCAAGTTGAGAGAAGAAATCGAAGTTAACTTTGGTGTTGGTGAAGACT 2254
CYP52A2A  2201 GCCAGAAACCCAGAAGTTACCAACAAGTTGAGAGAAGAAATTGAGGACAAGTTTGGACTCGGTGAGAATG 2270
CYP52A2B  2074 GCCAGAAACCCAGAGGTGACCAACAAGTTGAGAGAAGAAATCGAGGACAAGTTTGGTCTTGGTGAGAATG 2143
CYP52A3A  2182 TCAAGAAACCCTGAGGTGTTTGCTAAGTTGAGAGAGGAGGTGGAAAACAGATTTGGACTCGGTGAAGAAG 2251
CYP52A3B  1969 TCGAGAAACCCTGAAGTGTTTGCCAAGTTGAGAGAGGAGGTGGAAAACAGATTTGGACTCGGCGAAGAGG 2038
CYP52A5A  2050 GCCAGACACCCAGAGATCTGGGCCAAGTTGAGAGAGGAAATTGAACAACAGTTTGGTCTTGCAGAAGACT 2159
CYP52A5B  2129 GCCAGAAACCCACACATCTGGGCCAAGTTGAGAGAGGAAATTGAACAGCAGTTTGGTCTTGGAGAAGACT 2198
CYP52A8B  1436 GCCAGAAACCCACACATCTGGGCCAAGTTGAGAGAGGAAATTGAACAGCAGTTTGGTCTTGGAGAAGACT 1505
CYP52A8A  1439 GCCAGGAACCCACACATCTGGGCCAAGTTGAGAGAGGAAATTGAATCACACTTTGGGCTGGGTGAGGACT 2058
CYP52D4A  1712 GCCCGGAATGACCACATGTGGAGGAAGCTACGAGAGGAGGTT-------ATCCTGA---CGATGGGACCG 1771
                  * *  *    * *       *** *  **** **  *              **    *  *

CYP52A1A  2255 CCCGCGTTGAAGAAATTACCTTCGAAGCCTTGAAGAGATGTGAATACTTGAAGGCTATCCTTAACGAAAC 2324
CYP52A2A  2271 CTAGTGTTGAAGACATTTCCTTTGAGTCGTTGAAGTCCTGTGAATACTTGAAGGCTGTTCTCAACGAAAC 2213
CYP52A2B  2144 CTCGTGTTGAAGACATTTCCTTTGAGTCGTTGAAGTCATGTGAATACTTGAAGGCTGTCATCAATGAAAC 2321
CYP52A3A  2252 CTCGTGTTGAAGAGATCTCGTTTGAGTCCTTGAAGTCTTGTGAGTACTTGAAGGCTGTCATCAATGAAGC 2108
CYP52A3B  2039 CTCGTGTTGAAGAGATCTCTTTTGAGTCCTTGAAGTCCTGTGAGTACTTGAAGGCTGTCATCAATGAAAC 2229
CYP52A5A  2160 CTCGTGTTGAAGAGATTACCTTTGAGAGCTTGAAGAGATGTGAGTACTTGAAAGCGTTCCTTAATGAAAC 2268
CYP52A5B  2199 CTCGTGTTGAAGAGATTACCTTTGAGAGCTTGAAGAGATGTGAGTACTTGAAAGCCGTGTTGAACGAAAC 1575
CYP52A8A  1506 CTCGTGTTGAAGAGATTACCTTTGAGAGCTTGAAGAGATGTGAGTACTTGAAGGCCGTGTTGAACGAAAC 2128
CYP52A5B  2059 CTCGTGTTGAAGAGATTACCTTTGAGAGCTTGAAGAGATGTGAGTACTTGAAAGCCGTGTTGAACGAAAC 1839
CYP52D4A  1772 TCCAG--TGATGAAATAACCGTGGCCGGGTTGAAGAGTTGCCGTTACCTCAAAGCAATCCTAAACGAAAC 1839
                     *** ** **  *  * *     ******   **    *** * ** **  *  * ** *** *
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Figure 15G

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CYP52A1A  2325 CTTGCGTATGTACCCATCTGTTCCTGTCAACTTTAGAACCGCCACCAGAGACACCACTTTGCCAAGAGGT 2394
CYP52A2A  2341 CTTGAGATTGTACCCATCCGTGCCACAGAATTTCAGAGTTGCCACCAAGAACACTACCCTCCCAAGAGGT 2410
CYP52A2B  2214 TTTGAGATTGTACCCATCCGTGCCACAGAATTTCAGAGTTGCCACCAAAAACACTACCCTTCCAAGGGTA 2283
CYP52A3A  2322 CTTGAGATTGTACCCATCGGTTCCACACAACTTTAGAGTTGCTACCAGAAACACTACCCTCCCAAGAGGT 2391
CYP52A3B  2109 CTTGAGATTGTACCCATCTGTTCCACACAACTTCAGAGTTGCCACCAGAAACACTACCCTTCCAAGAGGC 2178
CYP52A5A  2230 CTTGCGTATTTACCCAAGTGTCCCAAGAAACTTCAGAATCGCCACCAAGAACACGACATTGCCAAGGGGC 2299
CYP52A5B  2269 CTTGCGTGTTTACCCAAGTGTCCCAAGAAACTTCAGAATCGCCACCAAGAATACAACATTGCCAAGGGGT 2338
CYP52A8A  1576 TTTGAGATTACACCCAAGTGTCCCAAGAAACGCAAGATTTGCGATTAAAGACACGACTTTACCAAGAGGC 1645
CYP52A8B  2129 GTTGAGATTACACCCAAGTGTCCCAAGAAACGCAAGATTTGCGATTAAAGACACGACTTTACCAAGAGGC 2198
CYP52D4A  1840 TCTTCGACTATACCCAAGTGTGCCTAGGAACGCGAGATTTGCTACGAGGAATACGACGCTTCCTCGTGGC 1909
                  *  *  *  *****  ** **   **   ***  ** *  *  * ** **  * **  * **

CYP52A1A  2395 GGTGGTGCTAACGGTACCGACCCAATCTACATTCCTAAAGGCTCCACTGTTGCTTACGTTGTCTACAAGA 2464
CYP52A2A  2411 GGTGGTAAGGACGGGTTGTCTCCTGTTTTGGTGAGAAGGGTCAGACCGTTATTTACGGTGTCTACGCAG 2480
CYP52A2B  2284 GGTGGTAAGGACGGGTTATCTCCTGTTTTGGTCAGAAAGGGTCAAACCGTTATGTACGGTGTCTACGCTG 2353
CYP52A3A  2392 GGTGGTGAAGATGGATACTCGCCAATTGTCGTCAAGAAGGGTCAAGTTGTCATGTACACTGTTATTGCTA 2461
CYP52A3B  2179 GGTGGTAAAGACGGATGCTCGCCAATTGTTGTCAAGAAGGGTCAAGTTGTCATGTACACTGTCATTGGTA 2248
CYP52A5A  2300 GGTGGTTCAGACGGTACCTCGCCAATCTTGATCCAAAAGGGAGAAGCTGTGTCGTATGGTATCAACTCTA 2369
CYP52A5B  2339 GGTGGTCCAGACGGTACCCAGCCAATCTTGATCCAAAAGGGAGAAGGTGTGTCGTATGGTATCAACTCTA 2408
CYP52A8A  1646 GGTGGCCCCAACGGCAAGGATCCTATCTTGATCAGGAAGGATGAGGTGGTGCAGTACTCCATCTCGGCAA 1715
CYP52A8B  2199 GGTGGCCCCAACGGCAAGGATCCTATCTTGATCAGAAAGAATGAGGTGGTGCAATACTCCATCTCGGCAA 2268
CYP52D4A  1910 GGAGGTCCAGATGGATCGTTTCCGATTTTGATAAGAAAGGGCCAGCCAGTGGGGTATTTCATTTGTGCTA 1979
                  ** **    * **      ** *   *   **         **   **    *

CYP52A1A  2465 CCCACCGTTTGGAAGAATACTACGGTAAGGACGCTAACGACTTCAGACCAGAAAGATGGTTTGAACCATC 2534
CYP52A2A  2481 CCCACAGAAACCCAGCTGTTTACGGTAAGGACGCTCTTGAGTTTAGACCAGAGAGATGGTTTGAGCCAGA 2550
CYP52A2B  2354 CCCACAGAAACCCAGCTGTCTACGGTAAGGACGCCCTTGAGTTTAGACCAGAGAGGTGGTTTGAGCCAGA 2423
CYP52A3A  2462 CCCACAGAGACCCAAGTATCTACGGTGCCGACGCTGACGTCTTCAGACCAGAAAGATGGTTCGAGCCAGA 2318
CYP52A3B  2249 CCCACAGAGACCCAAGTATCTACGGTGCCGACGCCGACGTCTTCAGACCAGAAAGATGGTTCGAGCCATC 2439
CYP52A5A  2370 CTCATTTGGACCCTGTCTATTACGGCCCTGATGCTGCTGAGTTCAGACCAGAGAGATGGTTTGAGCCATC 2478
CYP52A5B  2409 CCCACTTAGATCCTGTCTATTATGGCCCTGATGCTGCTGATTTTAGACCGGAAAGATGGTTTGAACCATC 1785
CYP52A8A  1716 CTCAGACAAATCCTGCTTATTATGGCGCCGATGCTGCTGATTTTAGACCGGAAAGATGGTTTGAGCCATC 2338
CYP52A8B  2269 CTCAGACAAATCCTGCTTATTATGGCGCCGATGCTGCTGATTTTAGACCGGAAAGATGGGCTGCGTTAGA 2049
CYP52D4A  1980 CACACTTGAATGAGAAGGTATATGGGAATGATAGCCATGTGTTTCGACCGGAGAGATGGGCTGCGTTAGA 2049
                  * **.                ** **   **      *  **  **** ** ** ***   *    *

CYP52A1A  2535 TACTAAGAAGTTGGGCTGGGCTTATGTTCCATTCAACGGTGGTCCAAGAGTCTGCTTGGGTCAACAATTC 2604
CYP52A2A  2551 GACAAAGAAGCTTGGCTGGGCCTTCCTCCCATTCAACGGTGGTCCAAGAATCTGTTTGGGACAGCAGTTT 2620
CYP52A2B  2424 GACAAAGAAGCTTGGCTGGGCCTTCCTTCCATTCAACGGTGGTCCAAGAATTTGCTTGGGACAGCAGTTT 2493
CYP52A3A  2532 AACTAGAAAGTTGGGCTGGGCATACGTTCCATTCAATGGTGGTCCAAGAATCTGTTTGGGTCAGCAGTTT 2601
CYP52A3B  2319 AACTAGAAAGTTGGGCTGGGCATATGTTCCATTCAATGGTGGTCCAAGAATCTGTTTGGGTCAGCAGTTT 2388
CYP52A5A  2440 AACCAAAAAGCTCGGCTGGGCTTACTTGCCATTCAACGGTGGTCCAAGAATCTGTTTGGGTCAGCAGTTT 2509
CYP52A5B  2479 AACCAGAAAGCTCGGCTGGGCTTACTTGCCATTCAACGGTGGGCCACGAATCTGTTTGGGACAACAGTTT 2548
CYP52A8A  1786 AACTAGAAACTTGGGATGGGCTTTCTTGCCATTCAACGGTGGTCCAAGAATCTGTTTGGGACAACAGTTT 1855
CYP52A8B  2339 AACTAGAAACTTGGGATGGGCTTACTTGCCATTCAACGGTGGTCCAAGAATCTGCTTGGGACAACAGTTT 2408
CYP52D4A  2050 GGGCAAGAGTTTGGGCTGGTCGTATCTTCCATTCAACGGCGGCCCGAGAAGCTGCCTTGGTCAGCAGTTT 2119
                  *  *   * ** *** * *   * ******** ** ** **  **   **  * ** ** ** **

CYP52A1A  2605 GCCTTGACTGAAGCTTCTTATGTGATCACTAGATTGGCCCAGATGTTTGAAACTGTCTCATCTGATCCAG 2674
CYP52A2A  2521 GCCTTGACAGAAGCTTCGTATGTCACTGTCAGGTTGCTCCAGGAGTTTGCACACTTGTCTATGGACCCCA 2590
CYP52A2B  2494 GCCTTGACAGAAGCTTCGTATGTCACTGTCAGATTGCTCCAAGAGTTTGGACACTTGTCTATGGACCCAG 2671
CYP52A3A  2502 GCCTTGACCGAAGCTTCATACGTCACTGTCAGATTGCTCCAGGAGTTTGCACACTTGTCTATGGACCCAG 2658
CYP52A3B  2289 GCCTTGACTGAAGCTTCATACGTCACTGTCAGATTGCTCCAAGAGTTTGGAAACTTGTCCCTGGATCCAA 2458
CYP52A5A  2510 GCCTTGACGGAAGCTGGCTATGTGTTGGTTAGATTGGTGCAAGAGTTCTCCCACGTTAGGCTGGACCCAG 2579
CYP52A5B  2549 GCCTTGACCGAAGCTGGTTACGTTTTGGTCAGATTGGTGCAAGAGTTCTCCCACATTAGGCTGGACCCAG 2518
CYP52A8A  1856 GCTTTGACTGAAGCCGGTTACGTTTTGGTTAGACTTGTTCAGGAGTTTCCAAACTTGTCACAAGACCCCG 1925
CYP52A8B  2403 GCTTTGACCGAAGCCGGTTACGTTTTGGTTAGACTTGTTCAGGAATTCCCTAGCTTGTCACAGGACCCCG 2478
CYP52D4A  2120 GCAATCCTTGAAGCTTCGTATGTTTTGGCTCGATTGACACAGTGCTACACGACGATACAGCTTAG---AA 2186
                  **  *   *****   ** **       *  *   **   *          *
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Figure 15H

```
CYP52A1A  2675 GTCTCGAATACCCTCCACCAAAGTGTATTCACTTGACCATGAGTCACAACGATGGTGTCTTTGTCAAGAT 2744
CYP52A2A  2691 ACACCGAATATCCACCTAAGAAAATGTCGCATTTGACCATGTCGCTTTTCGACGGTGCCAATATTGAGAT 2633
CYP52A2B  2564 ACACCGAATATCCACCTAGGAAAATGTCGCATTTGACCATGTCCCTTTTCGACGGTGCTGATGTTAGAAT 2741
CYP52A3A  2672 ACACCGAATATCCACCAAAATTGCAGAACACCTTGACCTTGTCGCTCTTTGATGGTGCTGATGTTAGAAT 2528
CYP52A3B  2459 ACGCTGAGTACCCACCAAAATTGCAGAACACCTTGACCTTGTCACTCTTTGATGGTGCTGACGTTAGAAT 2649
CYP52A5A  2580 ACGAGGTGTACCCGCCAAAGAGGTTGACCAACTTGACCATGTGTTTGCAGGATGGTGCTATTGTCAAGTT 2688
CYP52A5B  2619 ATGAAGTGTATCCACCAAAGAGGTTGACCAACTTGACCATGTGTTTGCAGGATGGTGCTATTGTCAAGTT 1995
CYP52A8A  1926 AAACCAAGTACCCACCACCTAGATTGGCACACTTGACGATGTGCTTGTTTGACGGGGCATACGTCAAGAT 2548
CYP52A8B  2479 AAACTGAGTACCCACCACCTAGATTGGCACACTTGACGATGTGCTTGTTTGACGGGGCATACGTCAAGAT 2548
CYP52D4A  2187 CTACCGAGTACCCACCAAAGAAACTCGTTCATCTCACGATGAGTCTTCTCAACGGGGTGTACATCCGAAC 2256
                     ** ** **              * **  **        * ** *     *

CYP52A1A  2745 GTAA-AGTAGTCGATGCTGGGTATTCGATTACATGT--GTATAGGAAGATTTTGGTTTTTTATTCGTTCT 2811
CYP52A2A  2761 GTATTAGAGGGTCATGTGTTATTTT-GATTGTTTA-----GTTTGTAATTACTGATTAGGTTAATTCATG 2824
CYP52A2B  2634 GTATTAGAGGATCATGTGTTATTTTTGATTGGTTTAGTCTGTTTGTAGCTATTGATTAGGTTAATTCACG 2703
CYP52A3A  2742 GTACTAAGGTTGCTTTTCCTTGCTAATTTTCTTCTGTATAGCTTGTGTATTTAAATTGAATCGGCAATTG 2811
CYP52A3B  2529 GTTCTAAGGTTGCTTATCCTTGCTAGTGTTATT---TATAGTTTGTGTATTTAAATTGAATCGGCGATTG 2595
CYP52A5A  2650 TGACTAGCGGCGTGGTGAATGCGTTTGATTTTGTA---GTTTCTGTTTGCAGTAATGAGATAACTATTCA 2716
CYP52A5B  2689 TGACTAGTA-CGTA-TGAGTGCGTTTGATTTTGTA---GTTTCTGTTTGCAGTAATGAGATAACTATTCA 2753
CYP52A8A  1996 GTCATAGGTTTCCC---CATACAAGTAGTTCAGTA---ATTATACACTGTTTTTACTTTCTCTTCATACC 2059
CYP52A8B  2549 GCAATAGGTTT----------------------------------------------TGGTTTGACTTTGTTTCCATA-- 2580
CYP52D4A  2257 TAGAACTTGATTATGTGTTTATGGTTAATCGGGGCAAAGCACTGCAAGTCATTGATGTTTGTGGAAGCCC 2326

CYP52A1A  2812 TTTTTTTAATTTTTGTTAAATTAG-TTTAGAGATTTCATTAATACATAGATGGGTGCTATTTCCGAAACT 2880
CYP52A2A  2825 GATTGTTATTTATTGATAGGGGTT---------TGCGCGTGTTGCATTCACTTGGGATCGTTCCAGGTTG 2885
CYP52A2B  2704 GATTGTTATTTATTGATAGGGGGTGCGTGTGTGTGTGTGTGTTGCATTCACATGGGATCGTTCCAGGTTG 2773
CYP52A3A  2812 ATTTTTCTGATACCAATAACCGTA--------GTGCGATTTGACCAAAACCGTTCAAACTTTTTGTTCTC 2873
CYP52A3B  2596 ATTTTTCTGGTACTAATAACTGTA--------GTGGGTTTTGACCAAAACCGTTCAAACTTTTTTTTTT 2657
CYP52A5A  2717 GATAAGGCGAGTGGATGTACGTTT-TGTAAGAGTTT--CCT-TACAACCTTGGTGGGG-TGTGTGAGGTT 2781
CYP52A5B  2754 GATAAGGCGGGTGGATGTACGTTT-TGTAAGAGTTT--CCT-TACAACCCTGGTGGG--TGTGTGAGGTT 2817
CYP52A8A  2060 AAATGGACAAAAGTTTTAAGCATG-CCTAACAACGTGACCG-GACAATTGTGTCGCACTAGTATGTAACA 2127
CYP52A8B  2581 ------------------------------------------------------------TGCAAGT 2587
CYP52D4A  2327 AGCATTGGTGTTCCGGAGCATCAATAACCAATGTCTTGAAGGGTTTGATTTTCTTGACCTTCTTCTTCCT 2396

CYP52A1A  2881 TTACTTCTATCC--CCTGTATCCCTTATTATCCCTCTCAGTCACATGATTGCTGTAATTGTCGTGCAGGA 2948
CYP52A2A  2856 ATGTTTCCTTCCATCCT--GTCGAGTCAAAAGGAGTTTTGTTTTGTAACTCCGGACGATGTTTTAAATAG 2953
CYP52A2B  2774 TTGTTTCCTTCCATCCT--GTTGAGTCAAAAGGAGTTTTGTTTTGTAACTCCGGACGATGTCTTAGATAG 2841
CYP52A3A  2874 TCGTTGACG-----------TGCTCGCTCATCAGCACTGTTTGAAGACGAAAGA-GAAAATTTTTTGTA 2930
CYP52A3B  2658 TTTTCTTCCCCCTACCTTCGTTGCTCGCTCATCAGCACTGTTTGAAAACGAAAAAAGAAAATTTTTTGTA 2727
CYP52A5A  2782 GAGGTTGCATCTT-GGGGAGATTACACCTTTTG-CAGCTCTCCGTATACACTTGTACTCTTTGTAACCTC 2849
CYP52A5B  2818 G----CATCTTAG-GGAGAGATAGCACCTTTTG-CAGCTCTCCGTATACAGTTTTACTCTTTGTAACCTA 2881
CYP52A8A  2128 ATTGTAAAAATAG-TGTACACTAATTTGTGGTGGCCGGAGATAAATTACAGTTTGGTTTTGTGTAAACTC 2196
CYP52A8B  2588 AGTTCAGTAAT---TACACACTAATTTGTGGTGGCCGGCGATAAATTACCGTTTGGTTTTGTGTAAAAAT 2654
CYP52D4A  2397 GAGCTTCTTTCCG--TCAAACTTGTACAGAATGGCCATCATTTCAGGAACAACCA-CGTACGACGGCCGG 2463

CYP52A1A  2949 CACAAACTCCCTAACGGACTTAAACCATAAACAAGCTCAGAACCATAAGCCGACATCACTCCTTCTTCTC 3018
CYP52A2A  2954 AAGGTCGATCTCCATGTGATTGTTTTGACTGTTACTGTGATTATGTAATCTGCG-------GACGTTATA 3016
CYP52A2B  2842 AAGGTCGATCTCCATGTGATTGTTT-GACTGCTACTCTGATTATGTAATCTGTAAAGCCTAGACGTTATG 2910
CYP52A3A  2931 AACAACACTGTCCAAATTTACCCAACGTGAACCATTATG--CAAATGAGCGGCC---------CTTTCAA 2989
CYP52A3B  2728 AACAACATTGCCCAAACTTACCCAACGTGAACCATTATAACCAAATGAGCGGCG---------CTTTCAA 2788
CYP52A5A  2850 TATCAATCATGTGGGGGGGGGGTTCATTGTTTGGC-CATGGTGGTGCATGTTAAATCCGCC-AACTACC 2917
CYP52A5B  2882 TGCCAATCATGTGG------GGATTCATTGTTTGCC-CATGGTGGTGCATGCAAAATCCCCCCAACTACC 2944
CYP52A8A  2197 GCGGATATCTCTGGC-----AGTTTCTCTTCTCCGC-AGCAGCTTTGCCACGGGTTTGCTCTGGGGCCAA 2260
CYP52A8B  2655 TCGGACATCTCTGGT-----GGTTTCCCTTCTCCGC-AGCAGCTTTGCCACGGGTTTGCTCTGCGGCCAA 2718
CYP52D4A  2464 TACCGCATCTGGAGTA---TCTCGCCGTCGTTCAAGTAG--CACGAAAACAGCAACGACGTCACCATCTG 2528
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Figure 15I

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CYP52A1A  3019 TCTTCTCCAACCAATAGCATGGACAGACCCACCCTCCTATCCGAATCGAAGACCCTTATTGACTCCATAC 3088
CYP52A2A  3017 CAAGCATGTGATTGTGGTTTT------GCAGCCT-TTTGCACGACAAATGATCGTCAGACGATTACGTAA 3079
CYP52A2B  2911 CAAGCATGTGATTGTGGTTTTT-----GCAACCTGTTTGCACGACAAATGATCGACAGTCGATTACGTAA 2975
CYP52A3A  2990 CTGGTCGCTGGAAGCATTCGGG-----GATATCTACAACGCCCTTAAGTTTGAAACAGACATTGATTTAG 3054
CYP52A3B  2789 CTGGTCACTGGAGGCATTCGGG-----GATATCTACAACACCCTTAAGTTTGAGGAAGACATTGATTTAG 2853
CYP52A5A  2918 CAATCTCACATGAAACTCAAGCACACTAAAAAAAAAAAAAGATGTTGGGGGAAAACTT-TGGTTTCCCTTC 2986
CYP52A5B  2945 CAATCTCACATGAAACTCAAGCACACTAGAAAAAAAA--GATGTTGCGTGGGTTCTT-TTGATG------ 3005
CYP52A8A  2261 CAAATTCAAAAGGGGG----------AGAAACTTAACACCCCTTATCTCTCCACTC-TAGGTTGTAGCT 2318
CYP52A8B  2719 CAAATTCGAAAGGGGGGGGGGGGGGAGAAAGTTAACACCCCCTGTTCC--CACCG-TAGGCTGTAGCT 2785
CYP52D4A  2529 CTTCCCAATCTTGACACCC--------ACAGATACCCCTGCGGCTTCATGGATCAAAAACGTCGGCAACC 2590

CYP52A1A  3089 CCACCTGGAAGCCCCTCAAGCCACACACGTCATCCAGCCCACCCATCACCACATCCCTCTACTCGACAAC 3158
CYP52A2A  3080 TCTTTGTTA-----GAGGGGTAAAAAAAAACAAAATGGCAGCCAGAATTTCAAACATTCTGCAAACAATG 3144
CYP52A2B  2976 TCCATATTAT-TTAGAGGGGTAATAAAAAATAAA-TGGCAGCCAGAATTTCAAACATTTTGCAAACAATG 3043
CYP52A3A  3055 ACACCATAGA-TTTCAGCGGCATCAAGAATGACC----TTGCCCACATTTTGACGACCCCAACACCACTG 3119
CYP52A3B  2854 ACACCATAGA-TTTCAGCGGCATCAAGAATGACC----TTGTCCACATTTTGACAACCCCAACACCACTG 2918
CYP52A5A  2987 TTAGTAATT--AAACACTCTCACTCTCACTCTCACTCTCTCCACTCAGACAAACCAACCACCTGGGCTGC 3054
CYP52A5B  3006 TTGGGGAAA--ACTTTCGTTTCCTTTCTCAGTAATTAAACGTTCTCACTCAGACAAACCACCTGGGCTGC 3073
CYP52A8A  2319 CTTGTGGGG--ATGCAATTGTCGTACGTTTTTTATGTTTTGTCTAGACTTTGATGATTACGTTGGATTTC 2386
CYP52A8B  2786 CTTGTGGGGGGATGTAATTGTCGTACGTTTTC-ATGTTTGGCCCAGACTTTGATGATTACGTAGGCTTTC 2854
CYP52D4A  2591 CCGCGTATATGTCCATGTAATTCTCCATGGCCACCT--CCATCAACACACTGATGGAGCGACTGACGGTG 2658

CYP52A1A  3159 GTCCAAAGACGGCGAGTTCTGGTGTGCCCGGAAATCAGCCATCCCGGCCACATACAAGCAGCCGTTGATT 3228
CYP52A2A  3145 CAAAAAATGGGAAACTC--CAACAGACAAAA-AAAAAAACTCCGCAGCACTCCGAACCCACAGAACAATG 3211
CYP52A2B  3044 CAAAAGATGAGAAACTC--CAACAGAAAAAATAAAAAAACTCCGCAGCACTCCGAACCAACAAAACAATG 3111
CYP52A3A  3120 GAAGAATCACGCCAGA----AACTAGGCGATGGATCCAAGCCTGTGACCTTGCCCAATGGAGACGAAGTG 3185
CYP52A3B  2919 GAAGAATCGCGCCAGA----AACTAGGCGATGGATCCAAGCCTGTGGCCTTGCCCAATGGAGACGAAGTG 2984
CYP52A5A  3055 AGACAACCAGAAAAAAAAAAGAACAAAATCCAGATAGAAAAACAAAGGGCT-GGACAACCATAAAT-AAAC 3122
CYP52A5B  3074 AGACAACCAGAAAAAA------CAAAATCCAGATAGAAGAAGAAAGGGCT-GGACAACCATAAAT-AAAC 3135
CYP52A8A  2387 TTATGTCTGAGGCGTG----CTTGAAAGAAGTGTCAAAATGTGACAGGCG-ACGCTATTCGACAT-GAAC 2450
CYP52A8B  2855 TTATGTCTAAGGCGTG----CTTGACACAAGTGTCAAAAGGTGACAGGCG-ACGTTATTCGACAT-GAAC 2918
CYP52D4A  2659 CCACCACTGCCCTCGG------TTGAGTCAAGGCAGTATGATGCCGGGATCCAGTACTCCAATGGGAACC 2722

CYP52A1A  3229 GCGTGCATACTCGGCGAGCCCACAATGTGAGCCACGCATTCGGACCATGAAGCAAAGTACATTCACGAGA 3298
CYP52A2A  3212 GGG----CGCCAGAATTATTGACTATTGTGACTTTTTTA----------CGCTAACGCTCATTGCAGTG 3266
CYP52A2B  3112 GGGG--GCGCCAGAATTATTGACTATTGTGACTTTTTTTT--ATTTTTTCCGTTAACTTTCATTGCAGTG 3177
CYP52A3A  3186 GAGTTGAACCAAGCGTTCCTAGAAGTTACCACATTATTGTCGAATGAGTTTGACTTGGACCAATTGAACG 3255
CYP52A3B  2985 GAGTTGAACCAAGCGTTCCTAGAAGTTACCACATTATTGTCGAACGAGTTTGACTTGGACCAATTGAACG 3054
CYP52A5A  3123 AATCTAGGGTCTACTCCATCTTCCACTGTTTCTTCTTCTTCAGACTTAGCT-AACAAACAACTCACTTCA 3191
CYP52A5B  3136 AACCTAGGGTCCACTCCATCTTTCACT---TCTTCTTCTTCAGACTTATCT-AACAAACGACTCACTTCA 3201
CYP52A8A  2451 GCGAAAGGGTTATTTGCATCAATACGAG--GGGCTGACTCTAGTCTAGG---ATGGCAGTCCTAGGTTGC 2515
CYP52A8B  2919 GCAAAAGGGTAATTTGCATCGATACGAG--GGGTTGCCTCTGGTCTAAG---AAGGACCCCCCAGGTTGC 2983
CYP52D4A  2723 TCT-----GCACGGTGTCGCTGCAGTTTTTGAGGCGTATTTCGA--------TCCATGATCGTTCTTTGG 2779

CYP52A1A  3299 TCACGGGTGTTTCAG-TGTCGCAGATTGAGAAGTTCGACGATGGATGGAAGTACGATCTCGTTGCGGATT 3367
CYP52A2A  3267 TAGTGCGTCTTACACGG-------GGTATTGCTTTCTACAATGCAAGGGCA-CAGTTGAAGGTTTGCACC 3328
CYP52A2B  3178 AAGTGTGTTACACGGGGTGGTGATGGTGTTGGTTTCTACAATGCAAGGGCA-CAGTTGAAGGTTTCCACA 3246
CYP52A3A  3256 CGGCAGAGTTGTTATACTA-CGCTGGCGACATATCCTACAAGAAGGGCACATCAATCGCAGACAGTGCCA 3324
CYP52A3B  3055 CGGCCGAGTTGTTATACTA-CGCCGGCGACATATCCTACAAGAAGGGCACATCAATTGCCGACAGTGCCA 3123
CYP52A5A  3192 CCATGGATTACGCAGGCATCACGCGTGGCTCCATCAGATGG-CGAGGCCTTGAAGAAACTCG--CAGAATT 3258
CYP52A5B  3202 CCATGGATTACGCAGGTATCACGCGTGGGTCCATCAGAGG-CGAAGCCTTGAAGAAACTCG--CCGAGTT 3268
CYP52A8A  2516 AAACATGTTGCACCA-TATCCCTCCTGGAGTTGGTCGAC--CTCGCCTACGCC-ACCCTCA--GCGATCG 2579
CYP52A8B  2984 AAACATGTTGCACTG-CATCCCACTCAGAGTTGGTCGAC--CACGCCTACGCTTACCCTCA--GCGATCG 3048
CYP52D4A  2780 TGCTGTAGTATAACGAGCT--CTTGGTGTCCTTGAAATGGAACAGGTTGGATGTGTTGTTGAGTTTGTCT 2847
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Figure 15J

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CYP52A1A  3368 ACGACTTCGGTGGGTTGTTATCTAAACGAAGATTCTATGAGACGCAGCATGTGTTTCGGTTCGAGGATTG 3437
CYP52A2A  3329 TAACGTTGCCCCGTGTCAACTCAATTTGAC----------G--AGTAACTTCCTAAGCTCGAATTATGC 3385
CYP52A2B  3247 TAACGTTGCACCATATCAACTCAATTTATC----------CTCATTCATGTGATAAAAGAAGAGCCAAA 3305
CYP52A3A  3325 GATTGTCTTATTATTTGAGAGCAAACTAC--------------ATCTTGAACATACTTGGGTATTTGAT 3379
CYP52A3B  3124 GATTGTCTTACTATTTGAGAGCAAACTAC--------------ATCTTGAACATACTTGGGTACTTTAT 3178
CYP52A5A  3259 G-ACCATCCAGAACCAGCCATCCAGCT------TGAAAGAAATCAACACCGGCATCCAGAAGGACGACTT 3321
CYP52A5B  3269 G-ACCATCCAGAACCAGCCATCCAGCT------TGAAAGAAATCAACACCGGCATCCAGAAGGACGACTT 3331
CYP52A8A  2580 GCACTTTCCGTTGTTCAATATTTCTC----------------CTTCCCATTGTTCCAGGGGTTA--TC 2629
CYP52A8B  3049 GCACTTTCCGTTGCTCAATATTTCTCT------CCCCCCTGCTTCCCCCCATTGTTCCAGGGATTA--TC 3110
CYP52D4A  2848 GCGTGCTTGGTTTGCAAGTCTTCGATCG----------------AGCGTAGTGAGTAGACAGTTGGCGGG 2901

CYP52A1A  3438 TGCGTACGTCATGAGTGTGCCTTTTGATGGACCCAAGGAGGAAGGTTACGTGGTTGGGACGTACAGATCC 3507
CYP52A2A  3386 AGCT-CGTGCGTCAACCTATGTGCAGGAAAGAAAAAATCCAAAAA--AATCGAAA-ATGCGACTTTCGAT 3451
CYP52A2B  3306 AGGT-AAT-TGGCAGACCCCCCAAGGGGAACACGGAGTAGAAAGC--AATGGAAACACGCCCATGACAGT 3371
CYP52A3A  3380 TTCG-AAGCAGCGATTGGATTTGATAGTCACGGACAACGACGCGT--TGTTTGATAGTATTTTGAAAAGT 3446
CYP52A3B  3179 TTCG-AAGCAGCGATTGGATGTGATAGTCACCGACAACAACGCGT--TGTTTGATAATATTTTGAAAAGT 3245
CYP52A5A  3322 TGCC-AAGTTGTTGTCTGCCACCCCGAAAATCCCCACCAAGCACA--AGTTGAACGGCAACCACGAATT- 3387
CYP52A5B  3332 TGCC-AAGTTGTTGTCTTCCACCCCGAAAATCCACACCAAGCACA--AGTTGAATGGCAACCACGAATT- 3397
CYP52A8A  2630 AACA-ACGTTGCCGGCCTCCTC------------CCCAAATTA-----------CAAGAAAAATAAATT- 2674
CYP52A8B  3111 AACA-ACGTTGCCGGTCTCCTCTCCCCCCCCTCCCCCCAGTTAT-------GTACAAGAAAATTAAATT- 3171
CYP52D4A  2902 GGTGGTGGCTCGGGCTTTATTCTGTGTTTGTGTTTCCTTCTTAGT--CTTGGAATGACGCTGTTATCGAC 2969

CYP52A1A  3508 ATTGAAAGGTTGAGCTGGGGTAAAGACGGGGACGTGGA-GTGGACCATGG---CGACGACGTCGGATCCT 3573
CYP52A2A  3452 TTTGAATAAACCAAAAAGAAAAATGTCGCACTTTTTTC-----TCGCTCTCGCTCTCTCGACCCAAATCA 3516
CYP52A2B  3372 GCCATTTAGCCCACA---ACACATCTAGTATTCTTTTT-----TTTTTTGTGCGCAGGTGCACACCTGG 3433
CYP52A3A  3447 TTTGAAAAGATCTAC----AAGTTGATAAGCGTGTTGA-----ACGATATGATTGACAAGCAAAAGGTGA 3507
CYP52A3B  3246 TTTGAAAAGATCTAC----AAGTTGATAAGCGCGTTGA-----ACGATATGATTGACAAGCAAAAGGTGA 3306
CYP52A5A  3388 GTCTGAGGTCGCCATTGCCAAAAAGGAGTACGAGGTGTTGATTGCCTTGAGCGACGCCACAAAAGACCCA 3457
CYP52A5B  3398 GTCCGAAGTCGCCATTGCCAAAAAGGAGTACGAGGTGTTGATTGCCTTGAGCGACGCCACGAAAGAACCA 3467
CYP52A8A  2675 GTCGCACGGCACCGATCTGTCAAAGATACAGATAA--------ACCTTAAATCTGCAAAAACAAGACCCC 2736
CYP52A8B  3172 GTCGCACGGCACCGATACGTCAAAGATACAGAGAA--------ACCTTAA----------------TCC 3216
CYP52D4A  2970 GGTTCGTAGTATAAGTAGCGCCAATATGAGAATGTATA-----TCCGCATCACCCAAGACTCTTCAGCCT 3034

CYP52A1A  3574 GGTGGGTTTATCCCGCA-ATGGATAACTCGATTGAGCA-TCCCTGGAGCAATCGCAAAAGATGTGCCTAG 3641
CYP52A2A  3517 CAACAAATCCTCGCGCGCAGTATTTCGACGAAAC--CACAACAAATAAAAAAAACAAATTCTACACCACT 3584
CYP52A2B  3434 ACTTTAGTTATTGCCC-CATAAAGTTAACAATCT--CACCTTTGGCTCTCCCAGTGTCTCCGCCTCCAGA 3500
CYP52A3A  3508 CAAGCGACATCAACAGTCTAGCATTCATCAATTG--CATCAACTACTCGAGAGGTCAACTATTCTCCGCA 3575
CYP52A3B  3307 CAAGCGACATCAACAGTCTAGCATTTATCAACTG--CATCAACTACTCGAGGGGTCAACTATTCTCCGCA 3374
CYP52A5A  3458 ATCAAAGTGACCTCCCAGATCAAGATCTTGATTGACAAGTTCAAGGTGTACTTGT---TTGAGTTGCCTG 3524
CYP52A5B  3468 ATCAAAGTCACCTCCCAGATCAAGATCTTGATTGACAAGTTCAAGGTGTACTTGT---TTGAGTTGCCCG 3534
CYP52A8A  2737 TCCCCATAGCCTAGAAGCACCAGCAAGATGATGGAGCAACTCCTCCAGTACTGGTACATCGCACTCTCTG 2806
CYP52A8B  3217 CTCCCATAGCCTAGAAGCATCAAAAAGATGATTGAGCAACTCCTCCAGTACTGGTACATTGCACTCCCTG 3286
CYP52D4A  3035 GTTACAACGACTGAGGCTGTTGGCCGTGTGACCAATTGGTTTCTTTGGTGACCTAGATTGGTCCCGCAGG 3104

CYP52A1A  3642 TG---TATTAAACTACATACAGAAATAAAAACGTGTCTTGATTCATTGGTTT---GGTTCTTGTTGGGTT 3705
CYP52A2A  3585 T----CTTTTTCTTCACCAGTCAACAAAAAACAACAAATTATACACCATTTCAACGATTTTTGCTCTTAT 3650
CYP52A2B  3501 TG---CTCGTTTTACACCCTCGAGCTAACGACAACACAACACCCATGAGGGGAATGGGCAAAGTT----- 3562
CYP52A3A  3576 CA---CGAACTTTTGGG-ACTGGTTTTGTTTGGATTGGTCGACATCTATTTCAACCAGTTTGGCACATTA 3641
CYP52A3B  3375 CA---CGAACTTTTGGG-ACTGGTTTTGTTTGGATTGGTTGACAACTATTTCAACCAGTTTGGCTCATTA 3440
CYP52A5A  3525 AC---CAGAAGTTCTCCTACTCCATCGTGTCCAACTCCGTCAACATCGCCCCC-TGGACCTTGCTCGGGG 3590
CYP52A5B  3535 AC---CAGAAGTTCTCCTACTCCATCGTGTCCAACTCCGTTAACATTGCCCCC-TGGACCTTGCTCGGTG 3600
CYP52A8A  2807 TA---TGGTTCATCCTTCGCTACTTGGCTTCCCACGCACGAGCCGTCTACTTG-CGCCACAAGCTCGGCG 2872
CYP52A8B  3287 TA---TGGTTCATTCTCCGCTACGTGGCTTCCCACGCACGAACCATCTACTTG-CGCCACAAGCTCGGCG 3352
CYP52D4A  3105 GAAAGCAAGGGCTGCTAGGGGGGCATACCAAACAAGGTCGTGTAATCAGTATCTATGGTGCTACCATGTG 3174
```

Figure 15K

```
CYP52A1A  3706 CCGAGCCAATATTTCACATCATCTCCTAAATTCTCCAAGAATCCCAACGTAGCGTAGTCCAGCACGCCCT 3775
CYP52A2A  3651 AAATGCTATATAATGGTTTAATTCAACTCAGGTATGTTTAT-TTTACTGTTTTCAGCTCAAGTATGT--T 3727
CYP52A2B  3563 AAACACTTTTGGTTTCAATGATTCCTATTTGCTACTCTCTTGTTTTGTGTTTTGATTTGCACCATGT--G 3630
CYP52A3A  3642 GACAACTACAAGAAGGTATTGGCATTGATACTGAAGAACATCAGCGATGAAGACATCTTGATCATAC--A 3709
CYP52A3B  3441 GACAACTACAAGAAAGTATTGGCATTGATACTGAAGAACATCAGTGATGAAGATATCTTGATCGTAC--G 3508
CYP52A5A  3591 AGAAGTTGACCACGGGCTTGATCAACTTGGCCTTCCAGAACAACAAGCAGCACTTGGACGAGGTCATT-G 3659
CYP52A5B  3601 AGAAGTTGACCACGGGCTTGATCAACTTGGCGTTCCAGAACAACAAGCAGCACTTGGACGAAGTCATC-G 3669
CYP52A8A  2873 CGGCGCCATTCACGCACACCCAGTACGACGGCTGGTATGGGTTCAAGTTTGGGCGGGAGTTTCTCAA--G 2940
CYP52A8B  3353 CGGCGCCGTTCACGCACACCCAGTACGACGGATGGTATGGGTTCAAGTTTGGGCGGGAGTTTCTCAA--G 3420
CYP52D4A  3175 TGTGGTTGGGGGGAAATTCCCGCATTTTTGTGTAACGAAAGTTCTAGAAAGTTCTCGTGGGTTCTGAG-A 3243

CYP52A1A  3776 CTGAGATCTTATTTAATATCGACTTCTCAACCACCGGTGGAATC--CCGTTCAGACCATTGTTACCTGTA 3843
CYP52A2A  3718 CAAATACTAACTACTTTTGATGTTTGTCGCTTTTCTAGAATCAAAACAACGCCCACAACACGCCGAGCTT 3787
CYP52A2B  3631 AAATAAACGACAATTATATATACCTTT---TCGTCTGTCCTC----CAATGTCT-CTTTTTGCTGCCATT 3692
CYP52A3A  3710 CTTCCTCCCATCGACACTACAATTGTTTAAGCTGGTGTTGGACAA-GAAAGACGACGCTGCAGTTGAACA 3778
CYP52A3B  3509 CTTCCTCCCATCGACACTACAATTGTTTAAGCTGGTGTTGGATAA-GAAAGACGACGCCACTGTTGACCA 3577
CYP52A5A  3660 ACATCTTCAACGAGTTCATCGACAAGTTCTTTGGCAACACGGAG--CCGCAATTGAC-----CAACTTCT 3722
CYP52A5B  3670 ACATCTTCAACGAGTTCATCGACAAGTTCTTTGGCAACACGGAG--CCGCAATTGAC-----CAACTTCT 3732
CYP52A8A  2941 GCGAAGAAGATCGGGCGGCAGACGGACTTGGTGCATGCGCGGTT--CCGTGGCGG-------CATGGACA 3001
CYP52A8B  3421 GCGAAGAAGATTGGAAGGCAGACGGACTTGGTGCATGCGCGGTT--CCGTGGAGGGGG----CATGGATA 3484
CYP52D4A  3244 ATCTGCTGGAACCATCCACCCGCATTTCCGTTGCCAAAGTGGGAA-GAGCAATCAACCCACCCTGCTTTG 3312

CYP52A1A  3844 GTGTGTTTGCTCTTGTTCTTGATGACAATGATGTATTTGTCACGATACCTGAAATAATAAAACATCCAGT 3913
CYP52A2A  3788 GTCGAATAGACGGTTTGTTTACTCATTAGATGGTCCCAGATTACTTTTCAAGCCAAAGTCTCT-CGAGTT 3856
CYP52A2B  3693 TTGCTTTTTGCTTTTTGCTTTTGCACT---CTCTCCCACTCCCACAATCAGTGCAGCAACACA-CAA    3755
CYP52A3A  3779 GTTCTACAAGTACATCACTTCAACAGT--GTCACGAGACTACAACTCCAACATCGGCTCCACAGCCAAAG 3846
CYP52A3B  3578 GTTCTACAAGTACATCACCTCAACAGT--GTCGCAAGACTACAACTCCAACATCGGAGCCACAGCCAAAG 3645
CYP52A5A  3723 TGACCTTGTGCGGTGTGTTGGACGGGTTGATTGACCATGCC-AACTTCTTGAGCGTGTCCTCGCGGACCT 3791
CYP52A5B  3733 TGACCTTGTCCGGTGTGTTGGACGGGTTGATTGACCATGCC-AACTTCTTGAGCGTGTCCTCCAGGACCT 3801
CYP52A8A  3002 CCTTCTCGAGCTACACTTTCGGCATCCATATCATCCTTACC-CGGGACCCGGAGAACATCAAGGCGGTCT 3070
CYP52A8B  3485 CTTTCTCGAGCTATACTTTCGGCATCCATATCATTCTTACT-CGGGACCCGGAGAACATCAAGGCGGTCT 3553
CYP52D4A  3313 CCCAATCAGCCATTCCCCTGGGAATATAAATTCAAC                                  3348

CYP52A1A  3914 CATTGAGCTTATTACTCGTGAACTTATGAAAGAACTCATTCAAGCCGTTCCCAAAAAACCCAGAATTGAA 3983
CYP52A2A  3857 TTGTTTGCTGTTTCCCCAATTCCTAACTATGAAGGGTTTTTATAAGGTCCAAAGACCCCAAGGCATAGTT 3926
CYP52A2B  3756                                                                    3755
CYP52A3A  3847 ATGATATCGATTTGTCCAAAACCAAACTCAGTGGCTTTGAGGTGTTGACGAGTT                 3900
CYP52A3B  3646 ATGATATCGATTTGTCCAAAGCC                                            3663
CYP52A5A  3792 TCAAGATCTTCTTGAACTTGGACTCGTATGTGGAC                                 3825
CYP52A5B  3802 TCAAGATCTTCTTGAACTTGGACTCGTTTGTGGACAACTCGGACTTCTTGAACGACGTGGAGAACTACTC 3871
CYP52A8A  3071 TGGCGACGCAGTTCGATGACTTCTCGCTCGGTGGCAGGATCAGGTTCTTGAAGCCGTTGTTGGGGTATGG 3140
CYP52A8B  3554 TGGCGACGCAGTTCGATGACTTTTCG                                           3579
CYP52D4A  3349                                                                    3348

CYP52A1A  3984 GATCTTGCTCAACTGGTCATGCAAGTAGTAGATCGCCATGATCTGATACTTTACCAAGCTATCCTCTCCA 4053
CYP52A2A  3927 TTTTTGGTTCCTTCTTGTCGTG                                             3948
CYP52A2B  3756                                                                    3755
CYP52A3A  3901                                                                    3900
CYP52A3B  3669                                                                    3668
CYP52A5A  3827                                                                    3826
CYP52A5B  3872 CGACTTTTTGTACGACGAGCCGAACGAGTACCAGAACTT                            3910
CYP52A8A  3141 GATATTCACGTT                                                       3152
CYP52A8B  3580                                                                    3579
CYP52D4A  3349                                                                    3348
```

Figure 15L

```
CYP52A1A   4054 AGTTCTCCCACGTACGGCAAGTACGGCAACGAGCTCTGGAAGCTTTGTTGTTTGGGGTCATA 4215
CYP52A2A   3949                                                              3948
CYP52A2B   3756                                                              3755
CYP52A3A   3901                                                              3900
CYP52A3B   3669                                                              3668
CYP52A5A   3827                                                              3826
CYP52A5B   3911                                                              3910
CYP52A8A   3153                                                              3152
CYP52A8B   3580                                                              3579
CYP52D4A   3349                                                              3348
```

Figure 15M

```
CYP52A1A     1       MATQEIIDSVLPYL-------TKWYTVITAAVLVFLISTNIKNYV  38
CYP52A2A     1       MTVHDIIATY----------FTKWYVIVPLALIAYRVLDYFYGRY  35
CYP52A2B     1       MTAQDIIATY----------ITKWYVIVPLALIAYRVLDYFYGRY  35
CYP52A3A     1  MSSSPSFAQEVLATTSPYIEYFLDNYTRWYYFIPLVLLSLNFISLLHTRY  50
CYP52A3B     1  MSSSPSFAQEVLATTSPYIEYFLDNYTRWYYFIPLVLLSLNFISLLHTKY  50
CYP52A5A     1             MIEQLLEY----------WYVVVPVLYIIKQLLAYTKTRV  30
CYP52A5B     1             MIEQILEY----------WYIVVPVLYIIKQLIAYSKTRV  30
CYP52A8A     1             MLDQILHY----------WYIVLPLLAIINQIVAHVRTNY  30
CYP52A8B     1             MLDQIFHY----------WYIVLPLLVIIKQIVAHARTNY  30
CYP52D4A     1           MAISSLLSWD---------VICVVFICVCVYFGYEYCYTKY  32

CYP52A1A    39  KAKKLKCVDPPYLKDAGLTGILSLIAAIKAKNDGRLANFAD---EVFDEY  85
CYP52A2A    36  LMYKLGAKPFFQKQTDGCFGFKAPLELLKKKSDGTLIDFTL---QRIHDL  82
CYP52A2B    36  LMYKLGAKPFFQKQTDGYFGFKAPLELLKKKSDGTLIDFTL---ERIQAL  82
CYP52A3A    51  LERRFHAKPLGNFVRDPTFGIATPLLLIYLKSKGTVMKFAWGLWNNKYIV 100
CYP52A3B    51  LERRFHAKPLGNVVLDPTFGIATPLILIYLKSKGTVMKFAWSFWNNKYIV 100
CYP52A5A    31  LMKKLGAAPVTNKLYDNAFGIVNGWKALQFKKEGRAQEYND---YKFDHS  77
CYP52A5B    31  LMKQLGAAPITNQLYDNVFGIVNGWKALQFKKEGRAQEYND---HKFDSS  77
CYP52A8A    31  LMKKLGAKPFTHVQRDGWLGFKFGREFLKAKSAGRLVDLII---SRFHDN  77
CYP52A8B    31  LMKKLGAKPFTHVQLDGWFGFKFGREFLKAKSAGRQVDLII---SRFHDN  77
CYP52D4A    33  LMHKHGAREIENVINDGFFGFRLPLLLMRASNEGRLIEFSV---KRFESA  79
                                *          *

CYP52A1A    86  PN--HTFYLSVAGALKIVMTVDPENIKAVLATQFTDFSLGTRHAHFAPLL 133
CYP52A2A    83  DRPDIPTFTFPVFSINLVNTLEPENIKAILATQFNDFSLGTRHSHFAPLL 132
CYP52A2B    83  NRPDIPTFTFPIFSINLISTLEPENIKAILATQFNDFSLGTRHSHFAPLL 132
CYP52A3A   101  RDPKYKTTGLRIVGLPLIETMDPENIKAVLATQFNDFSLGTRHDFLYSLL 150
CYP52A3B   101  KDPKYKTTGLRIVGLPLIETIDPENIKAVLATQFNDFSLGTRHDFLYSLL 150
CYP52A5A    78  KNPSVGTYVSILFGTRIVVTKDPENIKAILATQFGDFSLGKRHTLFKPLL 127
CYP52A5B    78  KNPSVGTYVSILFGTKIVVTKDPENIKAILATQFGDFSLGKRHALFKPLL 127
CYP52A8A    78  ED----TFSSYAFGNHVVFTRDPENIKALLATQFGDFSLGSRVKFFKPLL 123
CYP52A8B    78  ED----TFSSYAFGNHVVFTRDPENIKALLATQFGDFSLGSRVKFFKPLL 123
CYP52D4A    80  PHPQNKTLVNRALSVPVILTKDPVNIKAMLSTQFDDFSLGLRLHQFAPLL 129
                          .. * .* ****.*.*** ***** *       **

CYP52A1A   134  GDGIFTLDGEGWKHSRAMLRPQFARDQIGHVKALEPHIQIMAKQIKLNQG 183
CYP52A2A   133  GDGIFTLDGAGWKHSRSMLRPQFAREQISHVKLLEPHVQVFFKHVRKAQG 182
CYP52A2B   133  GDGIFTLDGAGWKHSRSMLRPQFAREQISHVKLLEPHMQVFFKHVRKAQG 182
CYP52A3A   151  GDGIFTLDGAGWKHSRTMLRPQFAREQVSHVKLLEPHVQVFFKHVRKHRG 200
CYP52A3B   151  GDGIFTLDGAGWKHSRTMLRPQFAREQVSHVKLLEPHVQVFFKHVRKHRG 200
CYP52A5A   128  GDGIFTLDGEGWKHSRAMLRPQFAREQVAHVTSLEPHFQLLKKHILKHKG 177
CYP52A5B   128  GDGIFTLDGEGWKHSRSMLRPQFAREQVAHVTSLEPHFQLLKKHILKHKG 177
CYP52A8A   124  GYGIFTLDAEGWKHSRAMLRPQFAREQVAHVTSLEPHFQLLKKHILKHKG 173
CYP52A8B   124  GYGIFTLDGEGWKHSRAMLRPQFAREQVAHVTSLEPHFQLLKKHILKHKG 173
CYP52D4A   130  GKGIFTLDGPEWKQSRSMLRPQFAKDRVSHILDLEPHFVLLRKHIDGHNG 179
                * ******   **.**.*******.... *.  ****  .  *..    *
```

Figure 16A

```
CYP52A1A     1       MATQEIIDSVLPYL-------TKWYTVITAAVLVFLISTNIKNYV  38
CYP52A2A     1       MTVHDIIATY----------FTKWYVIVPLALIAYRVLDYFYGRY  35
CYP52A2B     1       MTAQDIIATY----------ITKWYVIVPLALIAYRVLDYFYGRY  35
CYP52A3A     1  MSSSPSFAQEVLATTSPYIEYFLDNYTRWYYFIPLVLLSLNFISLLHTRY  50
CYP52A3B     1  MSSSPSFAQEVLATTSPYIEYFLDNYTRWYYFIPLVLLSLNFISLLHTKY  50
CYP52A5A     1            MIEQLLEY----------WYVVVPVLYIIKQLLAYTKTRV  30
CYP52A5B     1            MIEQILEY----------WYIVVPVLYIIKQLIAYSKTRV  30
CYP52A8A     1            MLDQILHY----------WYIVLPLLAIINQIVAHVRTNY  30
CYP52A8B     1            MLDQIFHY----------WYIVLPLLVIIKQIVAHARTNY  30
CYP52D4A     1          MAISSLLSWD---------VICVVFICVCVYFGYEYCYTKY  32
                                .                   .

CYP52A1A    39 KAKKLKCVDPPYLKDAGLTGILSLIAAIKAKNDGRLANFAD---EVFDEY  85
CYP52A2A    36 LMYKLGAKPFFQKQTDGCFGFKAPLELLKKKSDGTLIDFTL---QRIHDL  82
CYP52A2B    36 LMYKLGAKPFFQKQTDGYFGFKAPLELLKKKSDGTLIDFTL---ERIQAL  82
CYP52A3A    51 LERRFHAKPLGNFVRDPTFGIATPLLLIYLKSKGTVMKFAWGLWNNKYIV 100
CYP52A3B    51 LERRFHAKPLGNVVLDPTFGIATPLILIYLKSKGTVMKFAWSFWNNKYIV 100
CYP52A5A    31 LMKKLGAAPVTNKLYDNAFGIVNGWKALQFKKEGRAQEYND---YKFDHS  77
CYP52A5B    31 LMKQLGAAPITNQLYDNVFGIVNGWKALQFKKEGRAQEYND---HKFDSS  77
CYP52A8A    31 LMKKLGAKPFTHVQRDGWLGFKFGREFLKAKSAGRLVDLII---SRFHDN  77
CYP52A8B    31 LMKKLGAKPFTHVQLDGWFGFKFGREFLKAKSAGRQVDLII---SRFHDN  77
CYP52D4A    33 LMHKHGAREIENVINDGFFGFRLPLLLMRASNEGRLIEFSV---KRFESA  79
                     .  .          *       .       *

CYP52A1A    86 PN--HTFYLSVAGALKIVMTVDPENIKAVLATQFTDFSLGTRHAHFAPLL 133
CYP52A2A    83 DRPDIPTFTFPVFSINLVNTLEPENIKAILATQFNDFSLGTRHSHFAPLL 132
CYP52A2B    83 NRPDIPTFTFPIFSINLISTLEPENIKAILATQFNDFSLGTRHSHFAPLL 132
CYP52A3A   101 RDPKYKTTGLRIVGLPLIETMDPENIKAVLATQFNDFSLGTRHDFLYSLL 150
CYP52A3B   101 KDPKYKTTGLRIVGLPLIETIDPENIKAVLATQFNDFSLGTRHDFLYSLL 150
CYP52A5A    78 KNPSVGTYVSILFGTRIVVTKDPENIKAILATQFGDFSLGKRHTLFKPLL 127
CYP52A5B    78 KNPSVGTYVSILFGTKIVVTKDPENIKAILATQFGDFSLGKRHALFKPLL 127
CYP52A8A    78 ED----TFSSYAFGNHVVFTRDPENIKALLATQFGDFSLGSRVKFFKPLL 123
CYP52A8B    78 ED----TFSSYAFGNHVVFTRDPENIKALLATQFGDFSLGSRVKFFKPLL 123
CYP52D4A    80 PHPQNKTLVNRALSVPVILTKDPVNIKAMLSTQFDDFSLGLRLHQFAPLL 129
                        .. *  .* ****.*.*** ***** *       **

CYP52A1A   134 GDGIFTLDGEGWKHSRAMLRPQFARDQIGHVKALEPHIQIMAKQIKLNQG 183
CYP52A2A   133 GDGIFTLDGAGWKHSRSMLRPQFAREQISHVKLLEPHVQVFFKHVRKAQG 182
CYP52A2B   133 GDGIFTLDGAGWKHSRSMLRPQFAREQISHVKLLEPHMQVFFKHVRKAQG 182
CYP52A3A   151 GDGIFTLDGAGWKHSRTMLRPQFAREQVSHVKLLEPHVQVFFKHVRKHRG 200
CYP52A3B   151 GDGIFTLDGAGWKHSRTMLRPQFAREQVSHVKLLEPHVQVFFKHVRKHRG 200
CYP52A5A   128 GDGIFTLDGEGWKHSRAMLRPQFAREQVAHVTSLEPHFQLLKKHILKHKG 177
CYP52A5B   128 GDGIFTLDGEGWKHSRSMLRPQFAREQVAHVTSLEPHFQLLKKHILKHKG 177
CYP52A8A   124 GYGIFTLDAEGWKHSRAMLRPQFAREQVAHVTSLEPHFQLLKKHILKHKG 173
CYP52A8B   124 GYGIFTLDGEGWKHSRAMLRPQFAREQVAHVTSLEPHFQLLKKHILKHKG 173
CYP52D4A   130 GKGIFTLDGPEWKQSRSMLRPQFAKDRVSHILDLEPHFVLLRKHIDGHNG 179
                    * ******   **.**.********.... *.  ****  .  *..    *
```

Figure 16A

```
CYP52A1A   383 TLRMYPSVPVNFRTATRDTTLPRGGGANGTDPIYIPKGSTVAYVVYKTHR 432
CYP52A2A   381 TLRLYPSVPQNFRVATKNTTLPRGGGKDGLSPVLVRKGQTVIYGVYAAHR 430
CYP52A2B   381 TLRLYPSVPQNFRVATKNTTLPRGGGKDGLSPVLVRKGQTVMYGVYAAHR 430
CYP52A3A   399 TLRLYPSVPHNFRVATRNTTLPRGGGEDGYSPIVVKKGQVVMYTVIATHR 448
CYP52A3B   399 ALRLYPSVPHNFRVATRNTTLPRGGGKDGCSPIVVKKGQVVMYTVIGTHR 448
CYP52A5A   376 TLRIYPSVPRNFRIATKNTTLPRGGGSDGTSPILIQKGEAVSYGINSTHL 425
CYP52A5B   376 TLRVYPSVPRNFRIATKNTTLPRGGGPDGTQPILIQKGEGVSYGINSTHL 425
CYP52A8A   371 TLRLHPSVPRNARFAIKDTTLPRGGGPNGKDPILIRKDEVVQYSISATQT 420
CYP52A8B   371 TLRLHPSVPRNARFAIKDTTLPRGGGPNGKDPILIRKNEVVQYSISATQT 420
CYP52D4A   358 TLRLYPSVPRNARFATRNTTLPRGGGPDGSFPILIRKGQPVGYFICATHL 407
                .**. **** * * * . ******** * *. . *   * * . ..

CYP52A1A   433 LEEYYGKDANDFRPERWFEPSTKKLGWAYVPFNGGPRVCLGQQFALTEAS 482
CYP52A2A   431 NPAVYGKDALEFRPERWFEPETKKLGWAFLPFNGGPRICLGQQFALTEAS 480
CYP52A2B   431 NPAVYGKDALEFRPERWFEPETKKLGWAFLPFNGGPRICLGQQFALTEAS 480
CYP52A3A   449 DPSIYGADADVFRPERWFEPETRKLGWAYVPFNGGPRICLGQQFALTEAS 498
CYP52A3B   449 DPSIYGADADVFRPERWFEPETRKLGWAYVPFNGGPRICLGQQFALTEAS 498
CYP52A5A   426 DPVYYGPDAAEFRPERWFEPSTKKLGWAYLPFNGGPRICLGQQFALTEAG 475
CYP52A5B   426 DPVYYGPDAAEFRPERWFEPSTRKLGWAYLPFNGGPRICLGQQFALTEAG 475
CYP52A8A   421 NPAYYGADAADFRPERWFEPSTRNLGWAFLPFNGGPRICLGQQFALTEAG 470
CYP52A8B   421 NPAYYGADAADFRPERWFEPSTRNLGWAYLPFNGGPRICLGQQFALTEAG 470
CYP52D4A   408 NEKVYGNDSHVFRPERWAALEGKSLGWSYLPFNGGPRSCLGQQFAILEAS 457
                   ** *.  ****** .  . ***...******* *******. **

CYP52A1A   483 YVITRLAQMFETVSSDPGLEYPPPKCIHLTMSHNDGVFVKM   523
CYP52A2A   481 YVTVRLLQEFAHLSMDPDTEYPPKKMSHLTMSLFDGANIEMY   522
CYP52A2B   481 YVTVRLLQEFGHLSMDPNTEYPPRKMSHLTMSLFDGANIEMY   522
CYP52A3A   499 YVTVRLLQEFAHLSMDPDTEYPPKLQNTLTLSLFDGADVRMY   540
CYP52A3B   499 YVTVRLLQEFGNLSLDPNAEYPPKLQNTLTLSLFDGADVRMF   540
CYP52A5A   476 YVLVRLVQEFSHVRLDPDEVYPPKRLTNLTMCLQDGAIVKFD   517
CYP52A5B   476 YVLVRLVQEFSHIRLDPDEVYPPKRLTNLTMCLQDGAIVKFD   517
CYP52A8A   471 YVLVRLVQEFPNLSQDPETKYPPPRLAHLTMCLFDGAHVKMS   512
CYP52A8B   471 YVLVRLVQEFPSLSQDPETEYPPPRLAHLTMCLFDGAYVKMQ   512
CYP52D4A   458 YVLARLTQCYTTIQLR-TTEYPPKKLVHLTMSLLNGVYIRTRT 499
                **  ** * .  .       ***     **.. ' *  .
```

Figure 16C

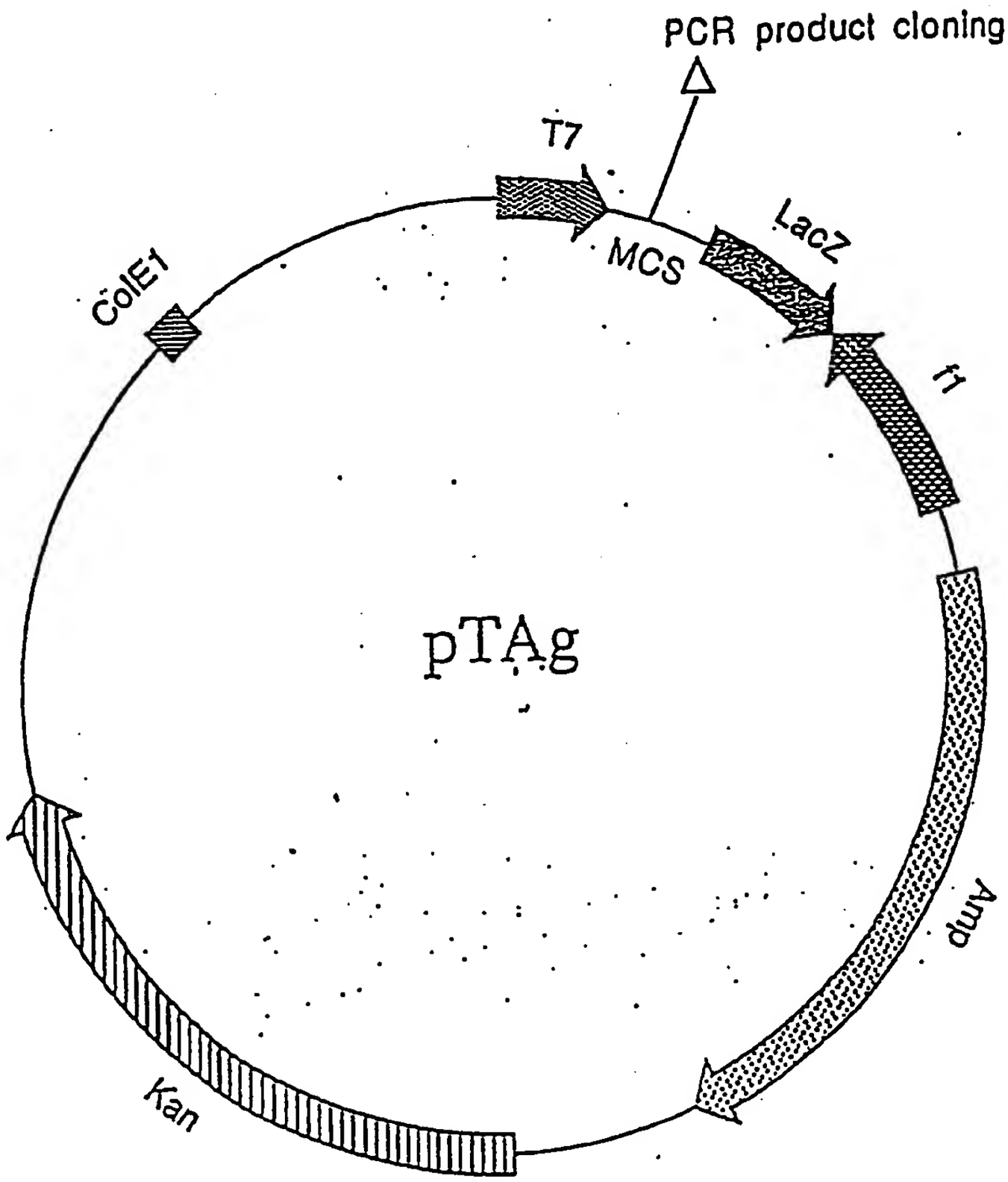

Figure 17

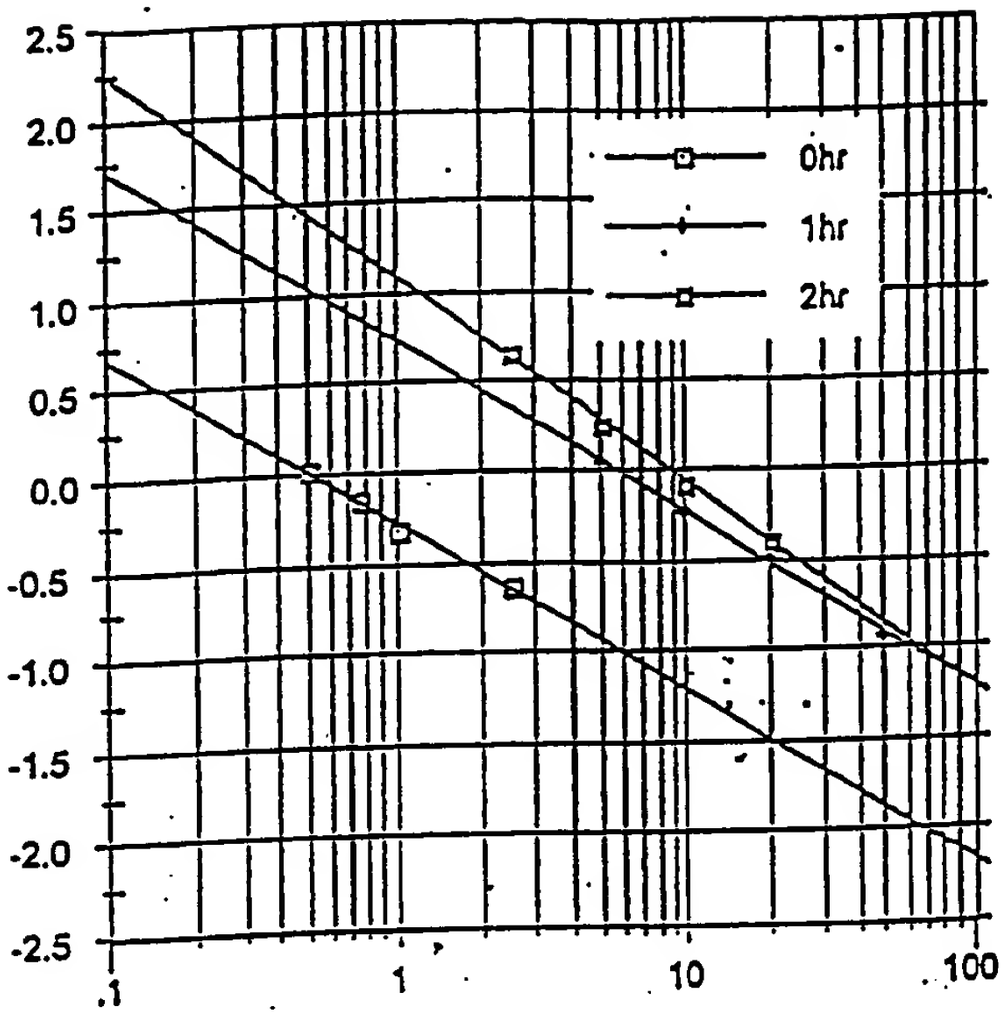
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
-2.5
.1
1
10
100
0hr
1hr
2hr
Log ratio U/C
conc competitor RNA pg

Figure 18

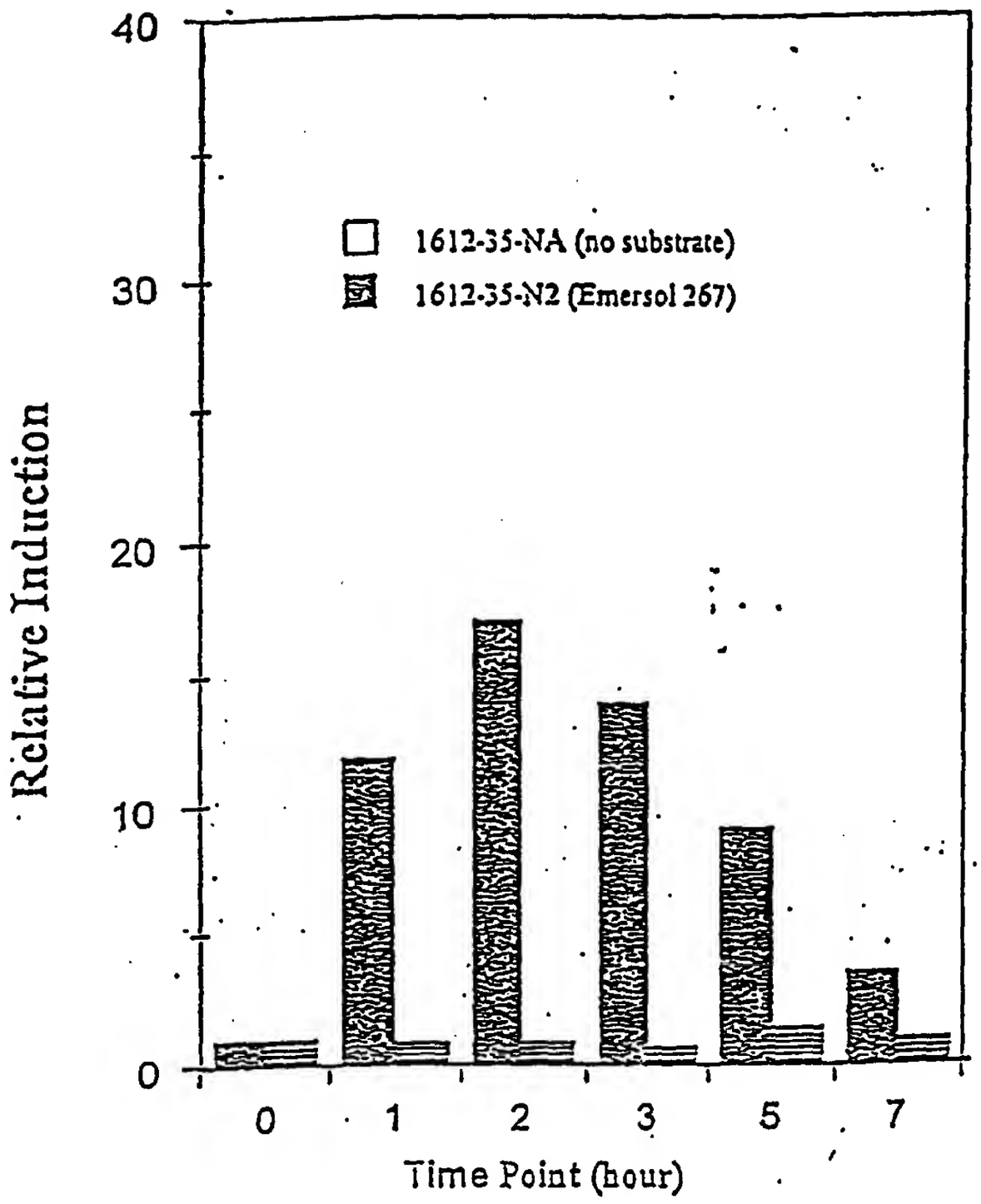
40
30
20
10
0
1612-35-NA (no substrate)
1612-35-N2 (Emersol 267)
Relative Induction
0
1
2
3
5
7
Time Point (hour)

Figure 19

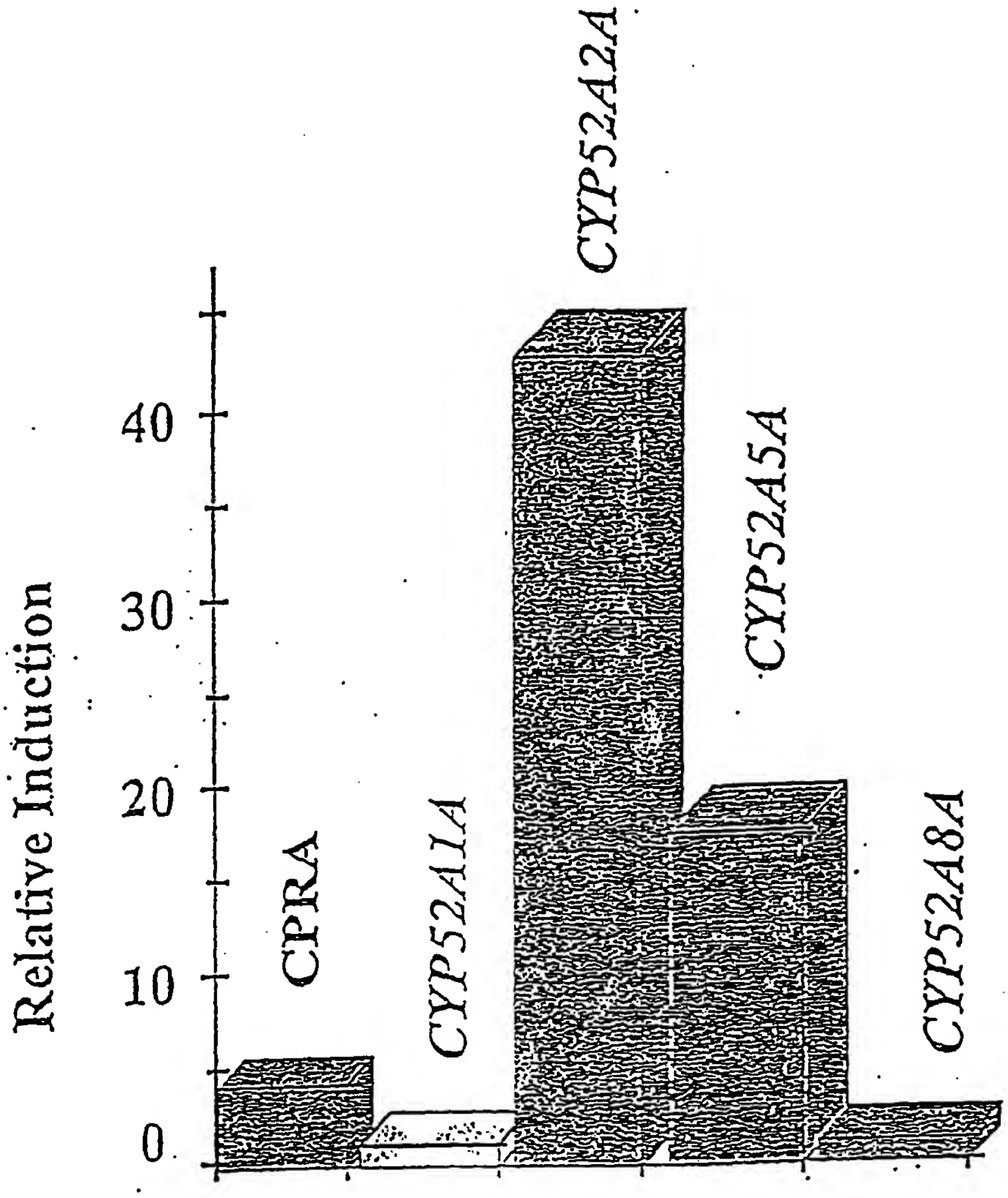
Relative Induction
0
10
20
30
40
CPRA
CYP52A11A
CYP52A5A
CYP52A8A

Figure 20

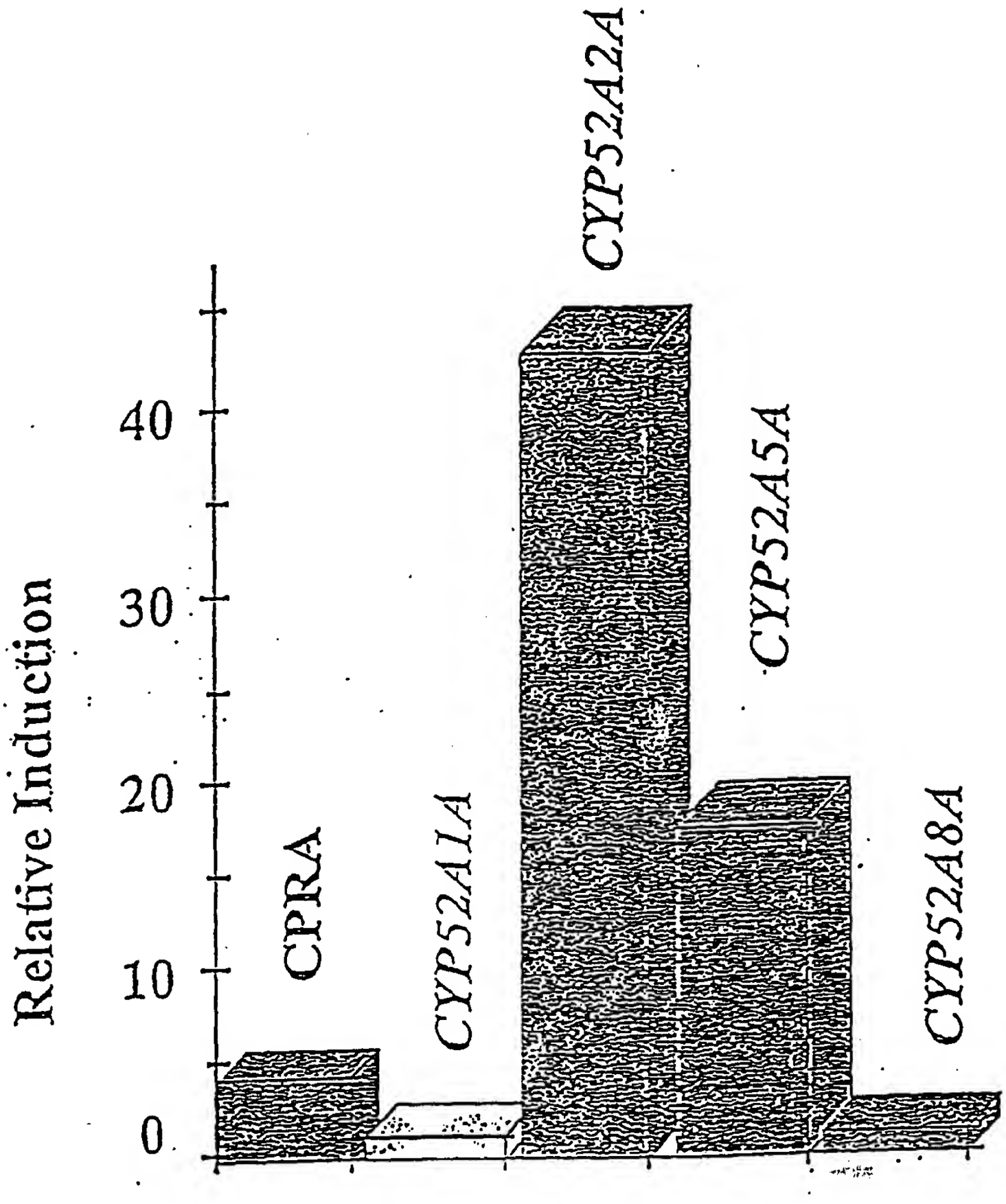
Relative Induction
0
10
20
30
40
CPRA
CYP52A11A
CYP52A5A
CYP52A8A

Figure 20

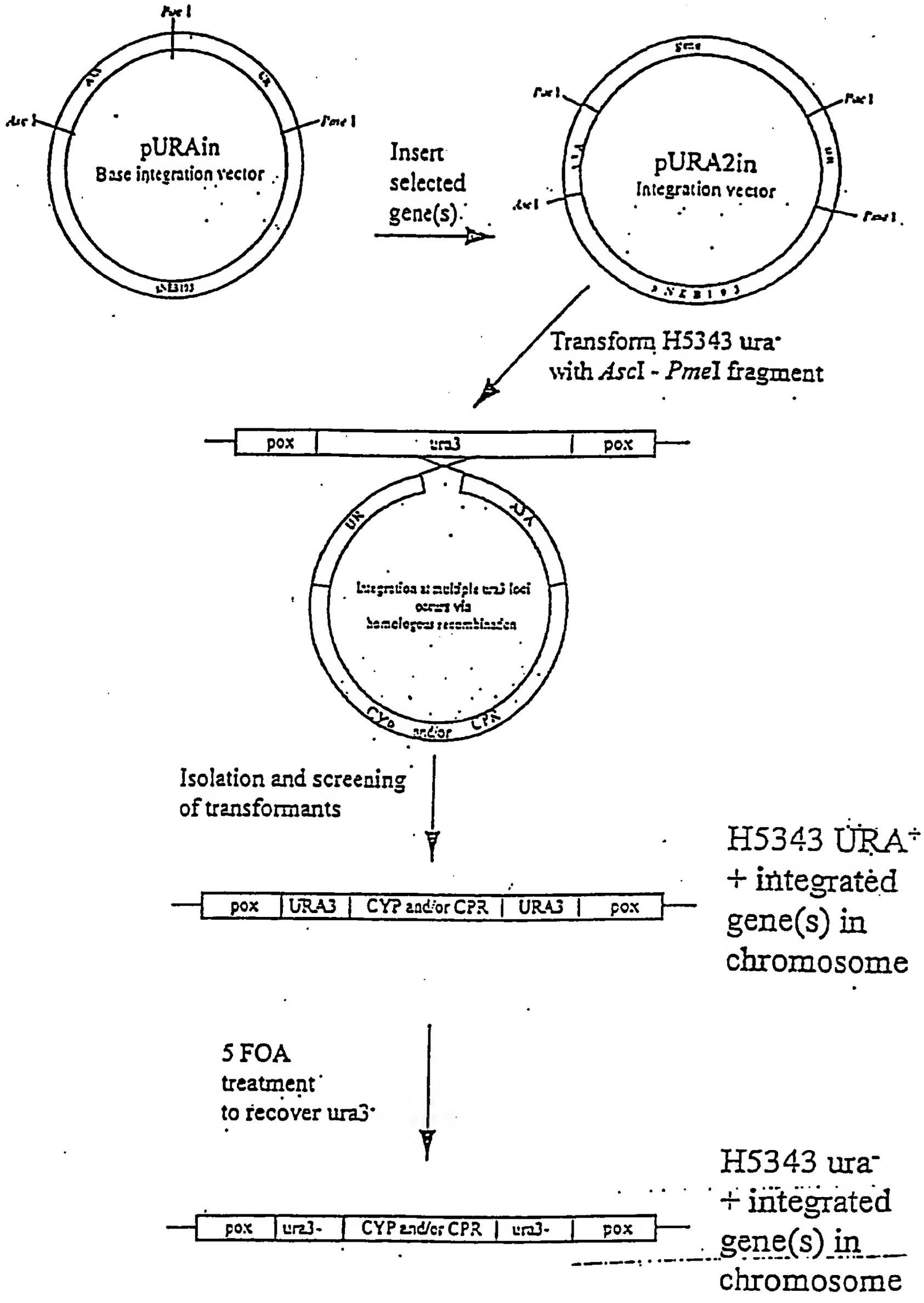
pURAin
Base integration vector
Insert selected gene(s)
pURA2in
Integration vector
Transform H5343 ura- with AscI - PmeI fragment
pox
ura3
pox
Isolation and screening of transformants
pox
URA3
CYP and/or CPR
URA3
pox
H5343 URA+ + integrated gene(s) in chromosome
5 FOA treatment to recover ura3-
pox
ura3-
CYP and/or CPR
ura3-
pox
H5343 ura- + integrated gene(s) in chromosome

Figure 21

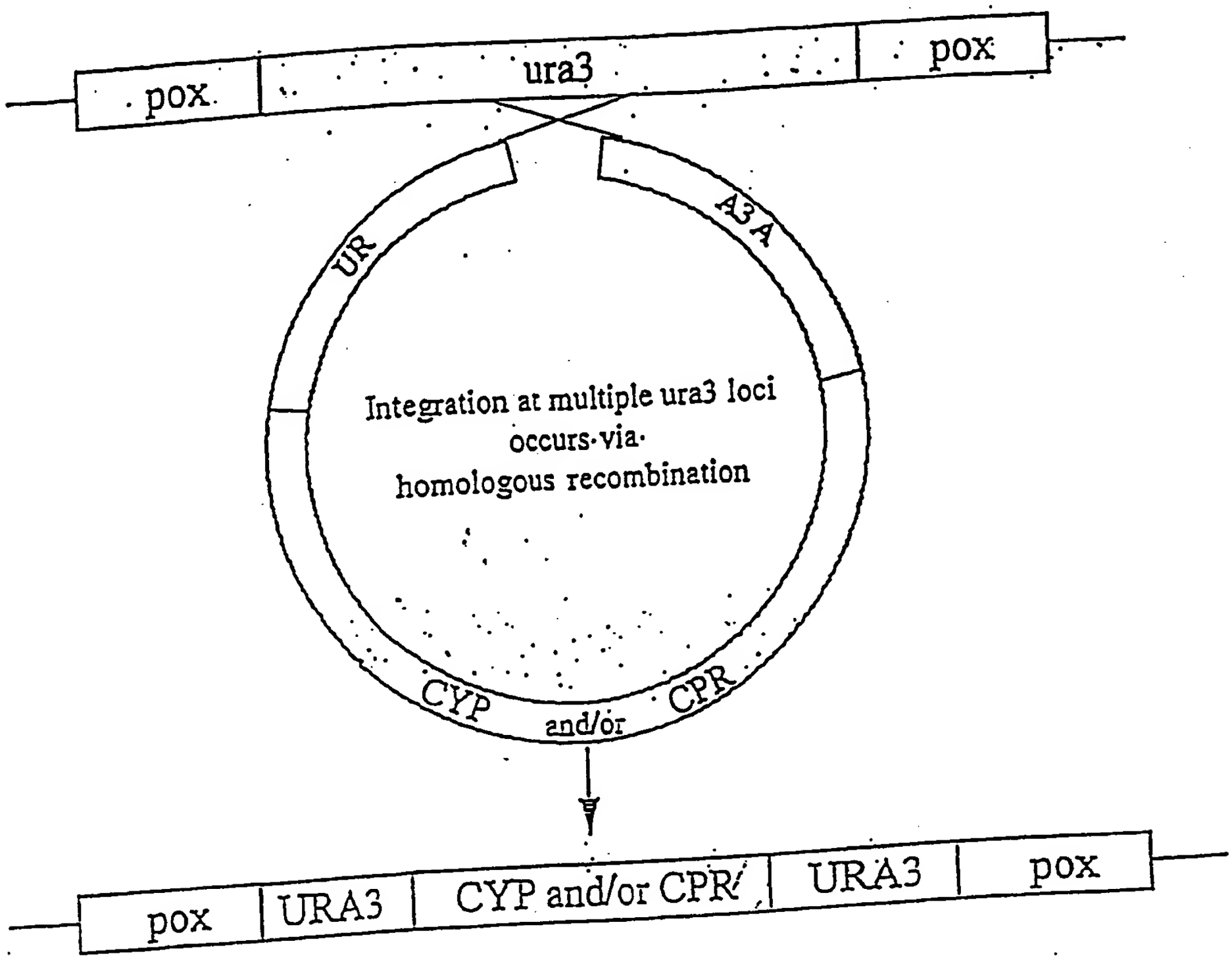
pox
ura3
pox
UR
A3A
Integration at multiple ura3 loci
occurs via
homologous recombination
CYP
and/or
CPR
pox
URA3
CYP and/or CPR
URA3
pox

Figure 22

Sequence Range: 1 to 1712

```
                10        20        30        40        50        60        70        80
            GGTACCGAGC TCACGAGTTT TGGGATTTTC GAGTTTGGAT TGTTTCGTTT GTTGATTGAA TTGACGAAAC CAGAGGTTTT

                90       100       110       120       130       140       150       160
            CAAGACAGAT AAGATTGGGC TTATCAAAAG GCAGTTTGAA ATATTTCAGG TGGTTTCGAA GATATCTTGA AGAAGATTGA

               170       180       190       200       210       220       230       240
            CGATTTGAAA TTTGAAGAAG TGGAGAAGAT CTGGTTTGGA TTGTTGGAGA ATTTCAAGAA TCTCAAGATT TACTCTAACG

               250       260       270       280       290       300       310       320
            ACGGGTACAA CGAGAATTGT ATTGAATTGA TCAAGAACAT GATCTTGGTG TTACAGAAGA TCAAGTTCTT GGACCAGACT

               330       340       350       360       370       380       390       400
            GAGAATGCCA CAGATATACA AGGCGTCATG TGATAAAATG GATGAGATTT ATCCCACAAT TGAAGAAAGA GTTTATGGAA

               410       420       430       440       450       460       470       480
            AGTGGTCAAC CAGAAGCTAA ACAGGAAGAA GCAAACGAAG AGGTGAAACA AGAAGAAGAA GGTAAATAAG TATTTTGTAT

               490       500       510       520       530       540       550       560
            TATATAACAA ACAAAGTAAG GAATACAGAT TTATACAATA AATTGCCATA CTAGTCACGT GAGATATCTC ATCGATTCCC

               570       580       590       600       610       620       630       640
            CAACTCCCAA GAAAAAAAAA AAGTGAAAAA AAAAATCAAA CCCAAAGATC AACCTCCCCA TCATCATCGT CATCAAACCC

               650       660       670       680       690       700       710       720
            CCAGCTCAAT TCGCAATGGT CAGCACAAAA ACATACACAG AAAGGGCATC AGCACACCCC TCCAAGGTTG CCCAACGTTT
                        M   V     S   T   K     T   Y   T     E   R   A   S     A   H   P     S   K   V     A   Q   R   L>

               730       740       750       760       770       780       790       800
            ATTCCGCTTA ATGGAGTCCA AAAAGACCAA CCTCTGCCCC TCGATCGACG TGACCACAAC CGCCGAGTTC CTTTCGCTCA
              F   R   L     M   E   S     K   K   T   N     L   C   A   S   I   D     V   T   T   T     A   E   F   L   S   L>

               810       820       830       840       850       860       870       880
            TCGACAAGCT CGGTCCCCAC ATCTGTCTCG TGAAGACGCA CATCGATATC ATGTCAGACT TCAGCTACGA GGGCAAGATT
              I   D   K   L     G   P   H     I   C   L     V   K   T   H     I   D   I     M   S   D     F   S   Y   E     G   K   I>

               890       900       910       920       930       940       950       960
            GAGCCGTTGC TTGTGCTTGC AGAGCGCCAC GGGTTCTTGA TATTCGAGGA CAGGAAGTTT GCTGATATCG GAAACACCGT
              E   P   L     L   V   L     A   E   R   H     G   F   L     I   F   E   D     R   K   F     A   D   I     G   N   T   V>

               970       980       990      1000      1010      1020      1030      1040
            GATGTTGCAG TACACCTCGG CGGTATACCG GATCGCGGCC TGGAGTGACA TCACGAACGC GCACGGAGTG ACTGCGAAGG
              M   L   Q     Y   T   S     G   V   Y   R     I   A   A   W   S   D     I   T   N   A     H   G   V     T   G   K>

              1050      1060      1070      1080      1090      1100      1110      1120
            GCGTCGTTGA AGGGTTGAAA CGCCGTCCCG AGGGGCTAGA AAAGCAAAGG GGCGTGTTGA TGTTGGCGGA GTTGTCGAGT
              G   V   V   E     G   L   K     R   G   A     E   G   V   E     K   E   R     G   V   L     M   L   A   E     L   S   S>

              1130      1140      1150      1160      1170      1180      1190      1200
            AAAGGCTCGT TGGCGCATGG TGAATATACC CGTGAGACGA TCGAGATTGC GAAGAGTGAT CGGGAGTTCG TGATTGGGTT
              K   G   S     L   A   H   G     E   Y   T     R   E   T     I   E   I   A     K   S   D     R   E   F     V   I   G   F>

              1210      1220      1230      1240      1250      1260      1270      1280
            CATCGCGCAG CGGGACATGG GGGGTAGAGA AGAAGGGTTT GATTGGATCA TCATGACGCC TGGTGTGGGG TTGGATGATA
              I   A   Q     R   D   M     G   G   R   E     E   G   F     D   W   I     I   M   T   P     G   V   G     L   D   D>

              1290      1300      1310      1320      1330      1340      1350      1360
            AAGGCGATGC GTTGGGCCAG CAGTATAGGA CTGTTGATGA GGTGGTTCTG ACTGGTACGG ATGTGATTAT TGTCGGGAGA
              K   G   D     A     L   G     Q     Q     Y     R     T   V   D     E     V   V   L     T   G   T     D   V   I   I     V   G   R>

              1370      1380      1390      1400      1410      1420      1430      1440
            GGGTTGTTTG GAAAAGGAAG AGACGCTGAG GTCGAGCGAA AGAGATACAG GGATGCTGGA TGGAAGGCAT ACTTGAAGAG
              G   L   F     G   K   G   R     D   P   E     V   E   G     K   R   Y   R     D   A   G     W   K   A     Y   L   K   R>

              1450      1460      1470      1480      1490      1500      1510      1520
            AACTGGTCAG TTAGAATAAA TATTGTAATA AATAGGTCTA TATACATACA CTAAGCTTCT AGGACGTCAT TGTAGTGTTC
              T   G   Q     L   E   *>

              1530      1540      1550      1560      1570      1580      1590      1600
            GAAGTTGTCT GCTAGTTTAG TTCTCATGAT TTCGAAAACC AATAACGCAA TGGATGTAGC AGGGATGGTG GTCAGTGGGT

              1610      1620      1630      1640      1650      1660      1670      1680
            TCCTGACAAA CGCAGAGTAC CCCCCCTCAA ACCACGTCAC ATTCGCCCTT TGCTTCATCC GCATCACTTG GTTGAACGTA

              1690      1700      1710
            TCCACGTACG AGTTGTAATA GATCTTGAAG AA
```

Figure 23

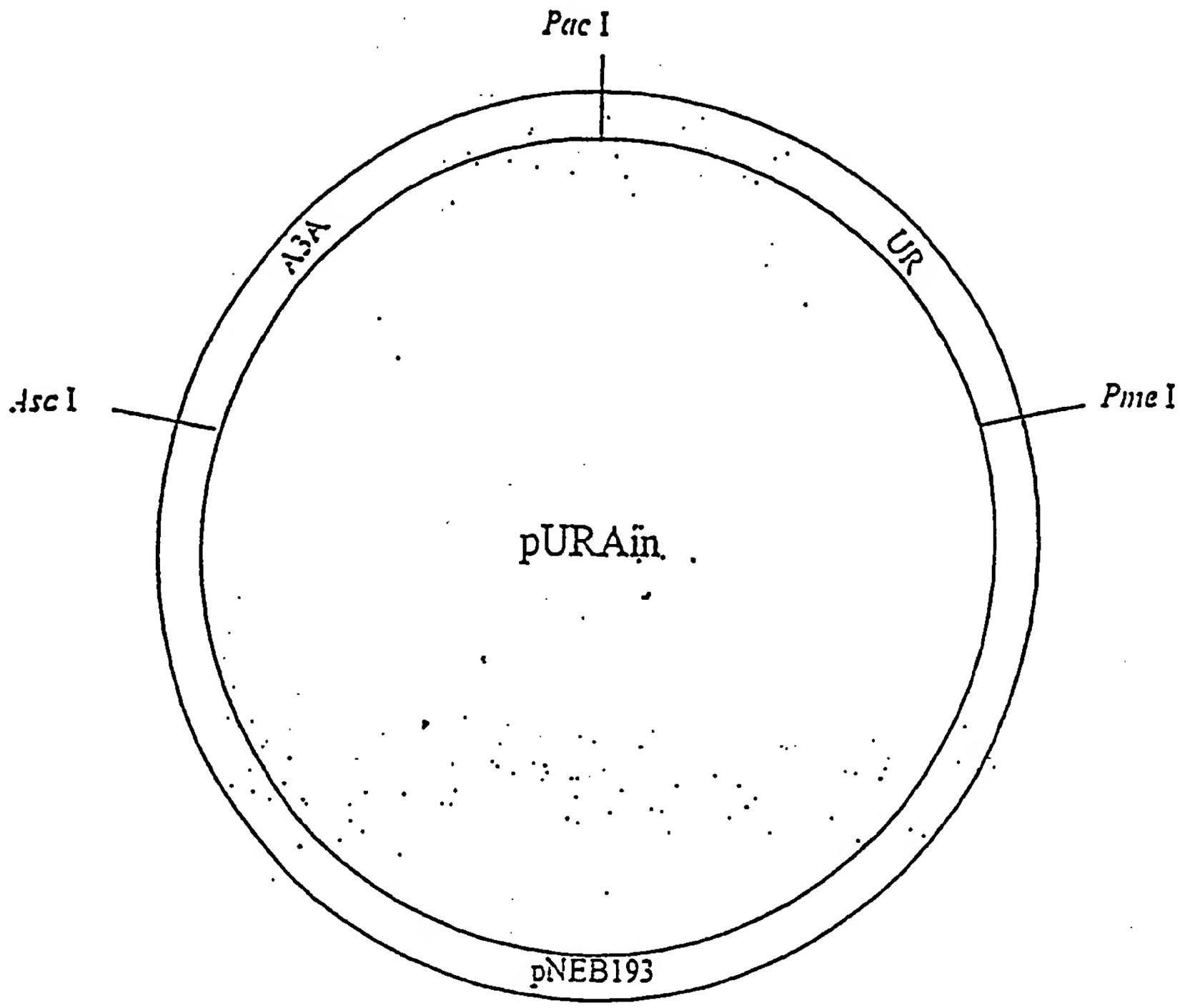

Figure 24

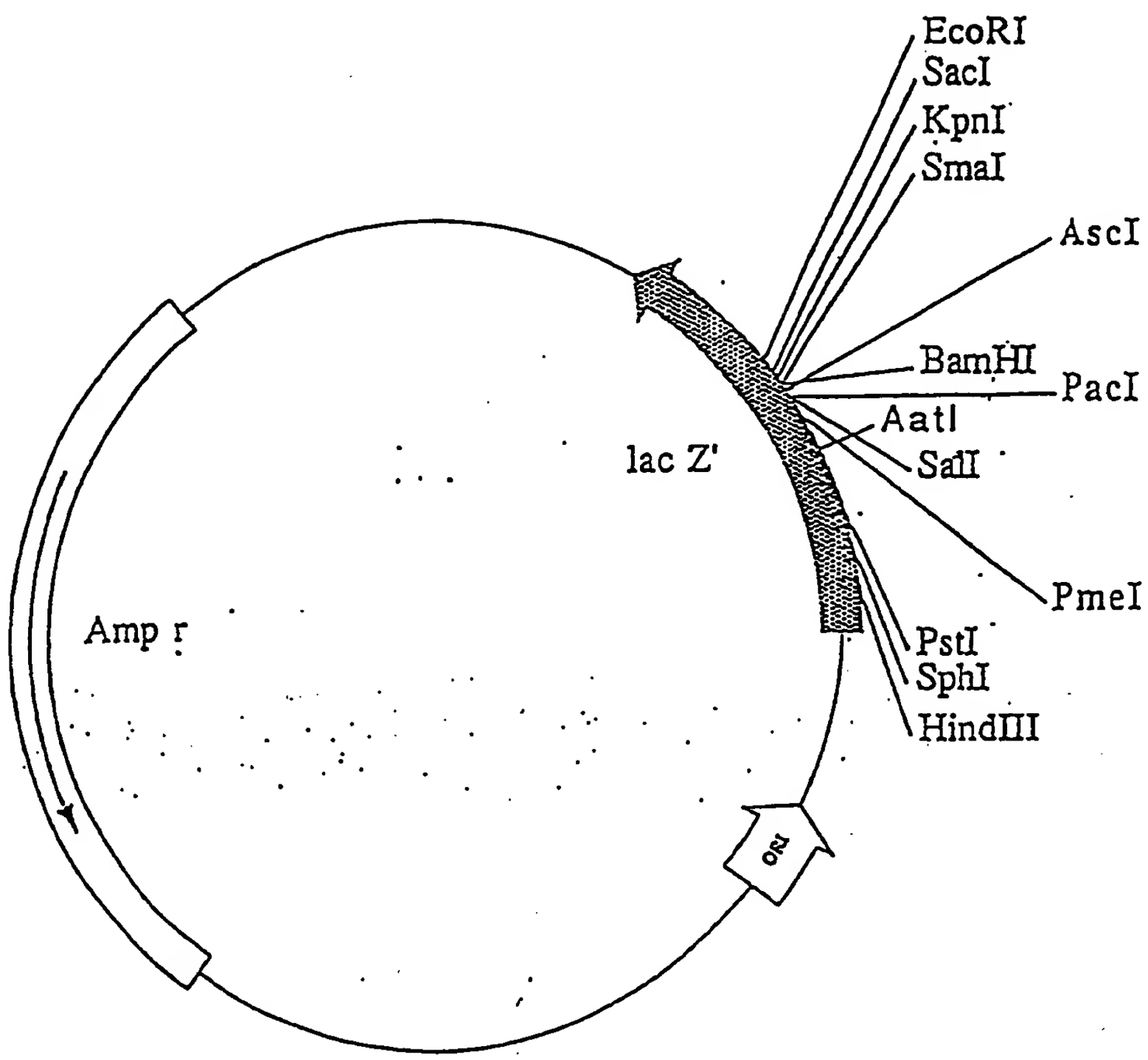
EcoRI
SacI
KpnI
SmaI
AscI
BamHI
PacI
AatI
SalI
PmeI
PstI
SphI
HindIII
lac Z'
Amp r
ORI

Figure 25

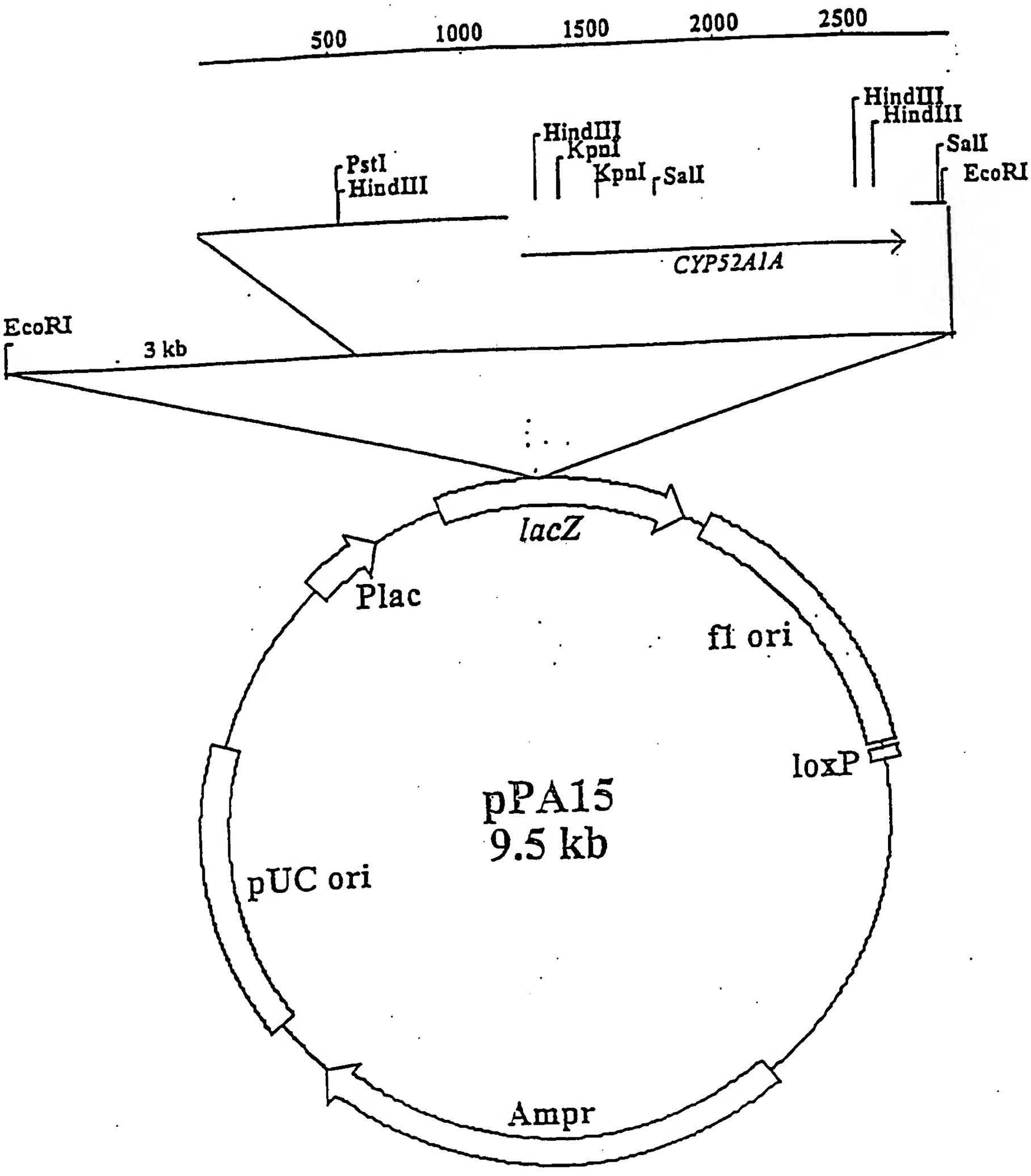
500
1000
1500
2000
2500
PstI
HindIII
HindIII
KpnI
KpnI
SalI
HindIII
HindIII
SalI
EcoRI
CYP52A1A
EcoRI
3 kb
lacZ
Plac
f1 ori
loxP
pPA15
9.5 kb
pUC ori
Ampr

Figure 26

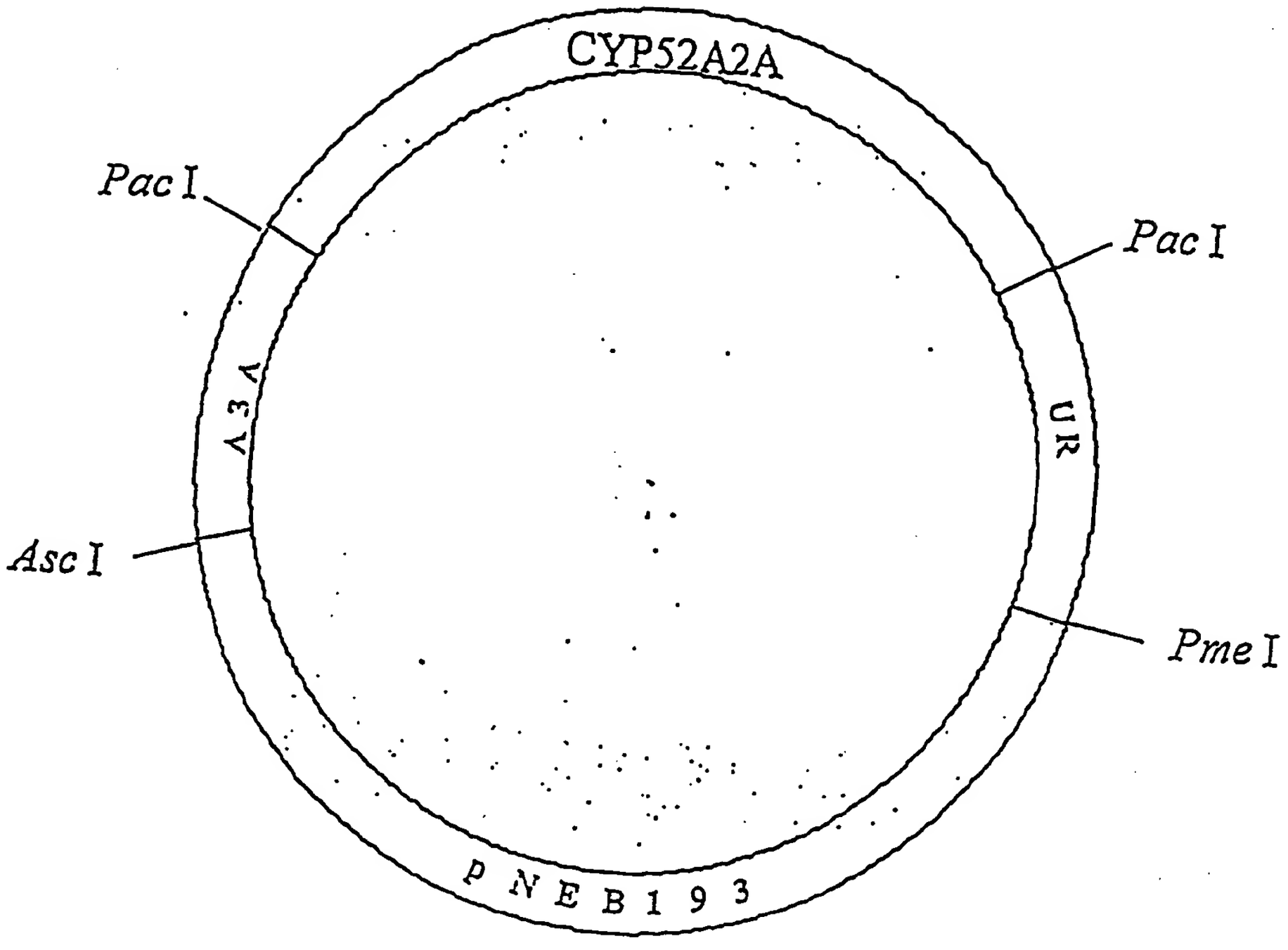

Figure 27

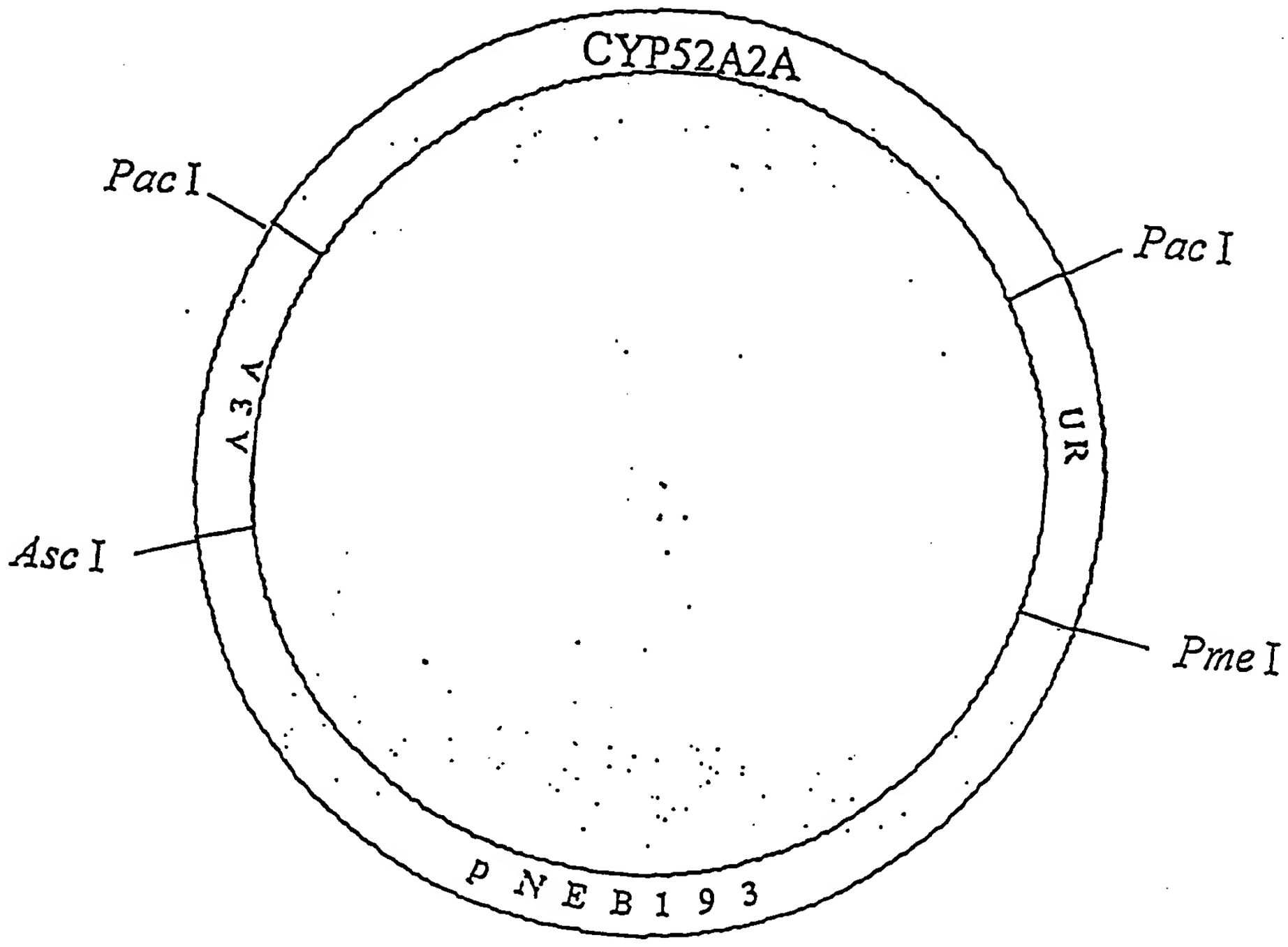

Figure 27

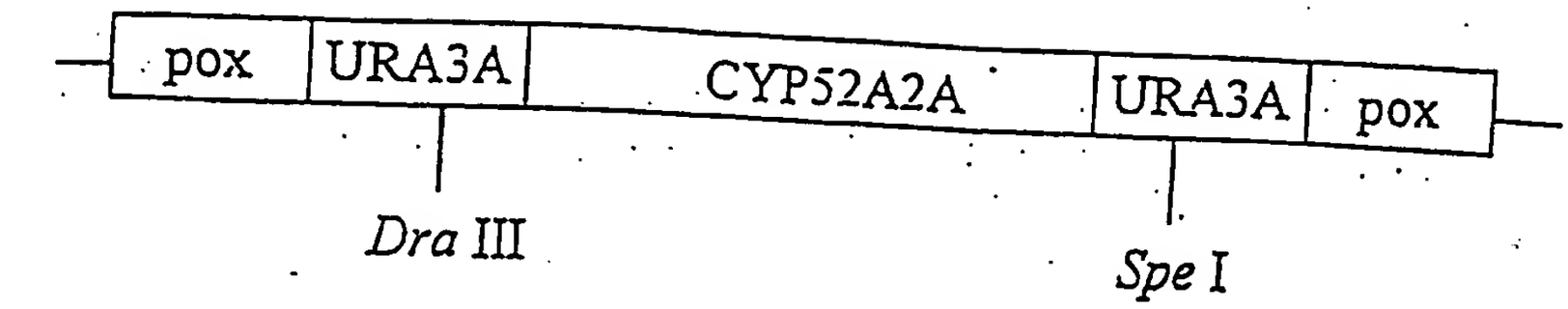
pox
URA3A
CYP52A2A
URA3A
pox
Dra III
Spe I
3.5(URA3A)or 3.3kb(URA3B)
pox
URA3A
CYP52A2A
URA3A
pox
Pac I
Pac I
2.2kb

Figure 28

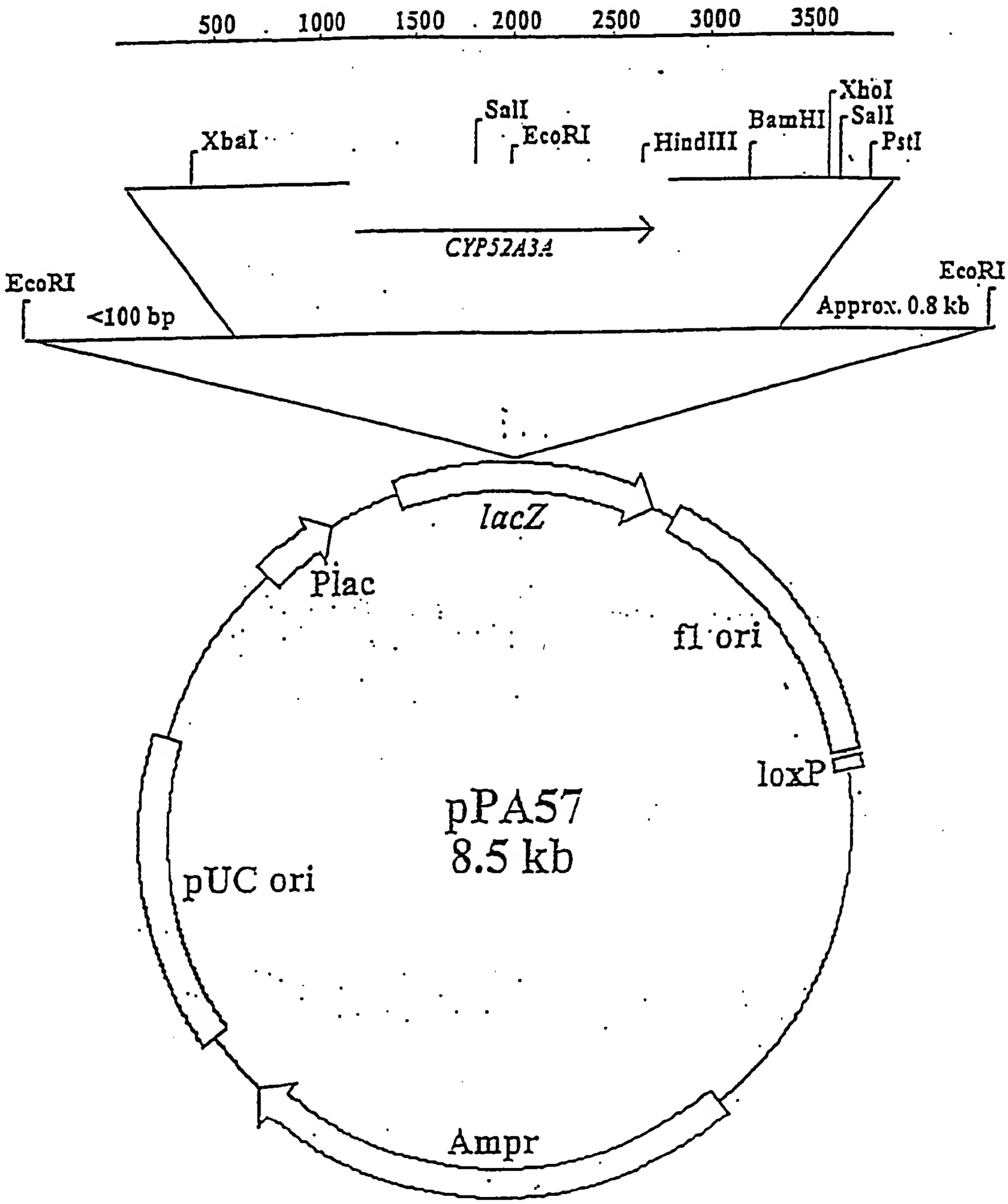
500
1000
1500
2000
2500
3000
3500
XbaI
SalI
EcoRI
HindIII
BamHI
XhoI
SalI
PstI
CYP52A3A
EcoRI
<100 bp
EcoRI
Approx. 0.8 kb
lacZ
Plac
f1 ori
loxP
pPA57
8.5 kb
pUC ori
Ampr

Figure 29

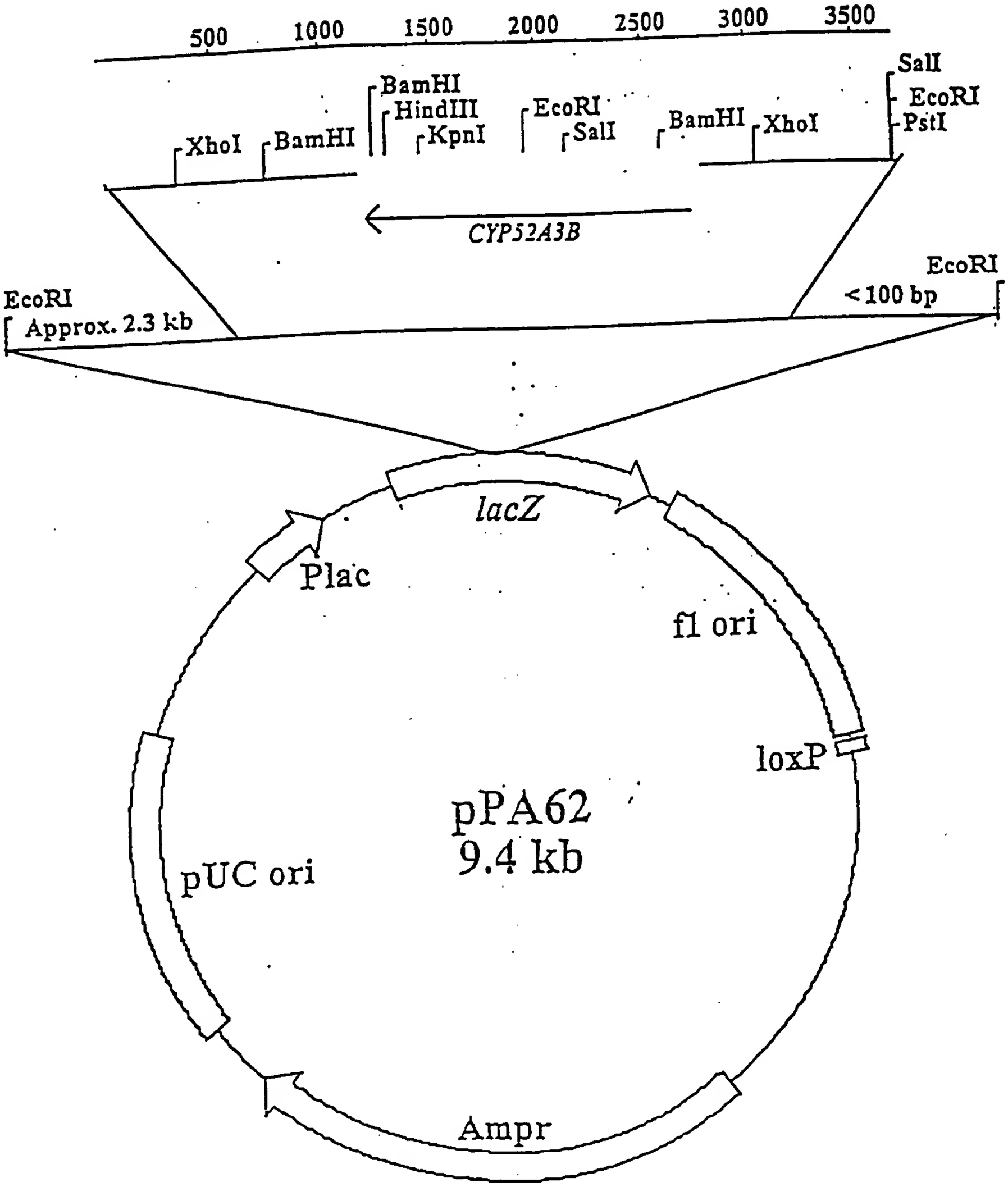
500
1000
1500
2000
2500
3000
3500
XhoI
BamHI
BamHI
HindIII
KpnI
EcoRI
SalI
BamHI
XhoI
SalI
EcoRI
PstI
CYP52A3B
EcoRI
Approx. 2.3 kb
EcoRI
< 100 bp
lacZ
Plac
f1 ori
loxP
pPA62
9.4 kb
pUC ori
Ampr

Figure 30

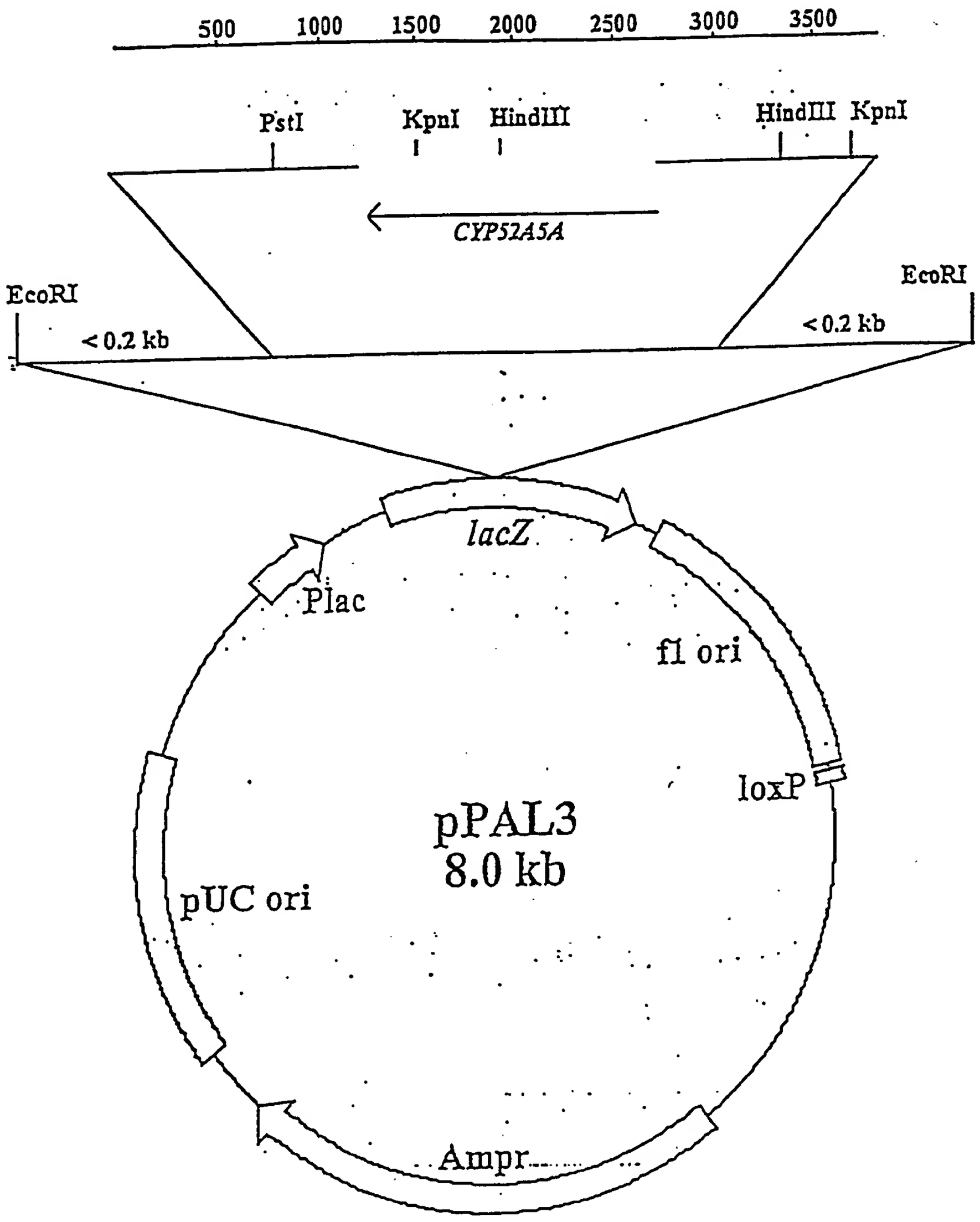
500
1000
1500
2000
2500
3000
3500
PstI
KpnI
HindIII
HindIII
KpnI
CYP52A5A
EcoRI
< 0.2 kb
EcoRI
< 0.2 kb
lacZ
Plac
f1 ori
loxP
pPAL3
8.0 kb
pUC ori
Ampr

Figure 31

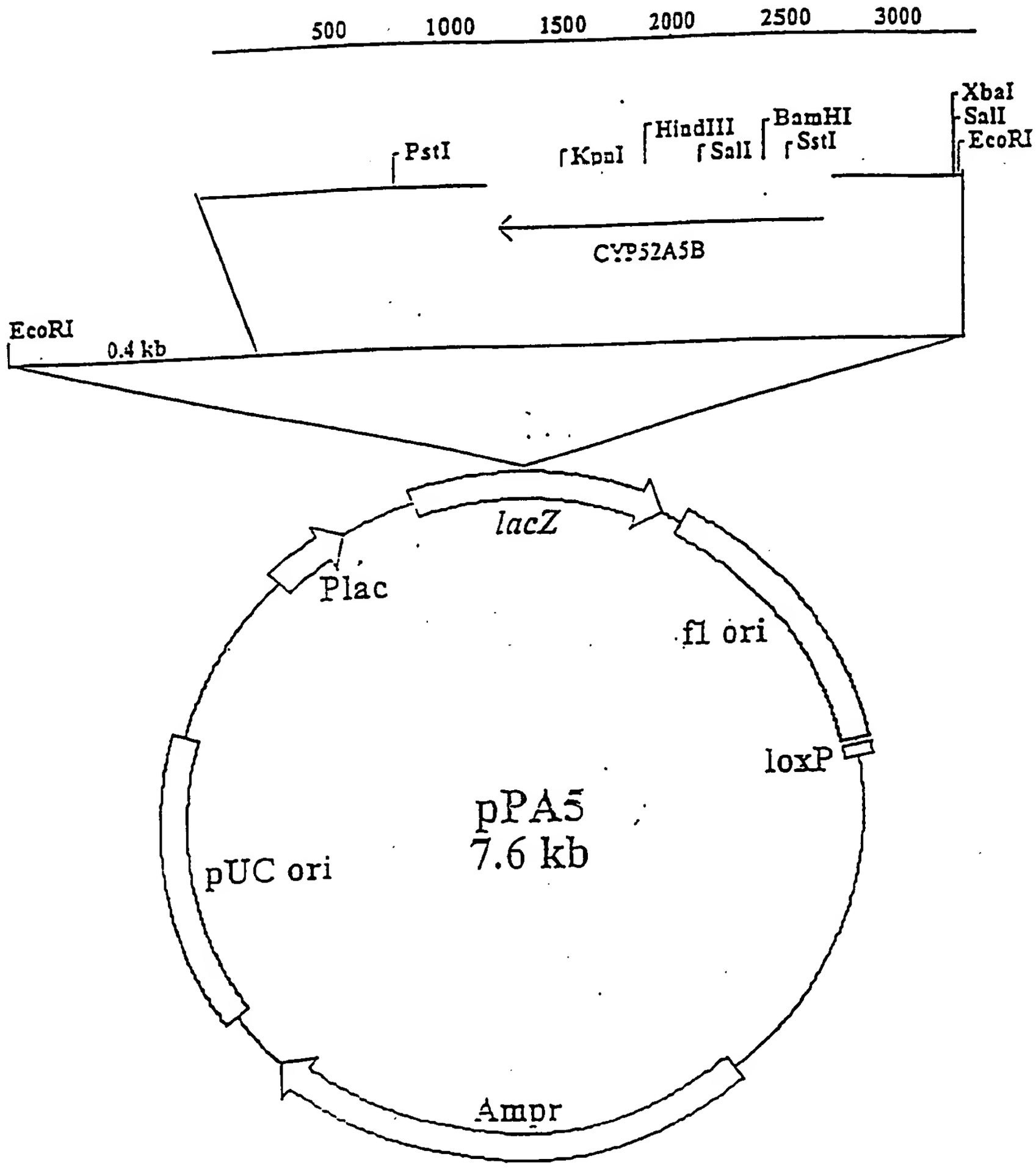
500
1000
1500
2000
2500
3000
PstI
KpnI
HindIII
SalI
BamHI
SstI
XbaI
SalI
EcoRI
CYP52A5B
EcoRI
0.4 kb
lacZ
Plac
f1 ori
loxP
pPA5
7.6 kb
pUC ori
Ampr

Figure 32

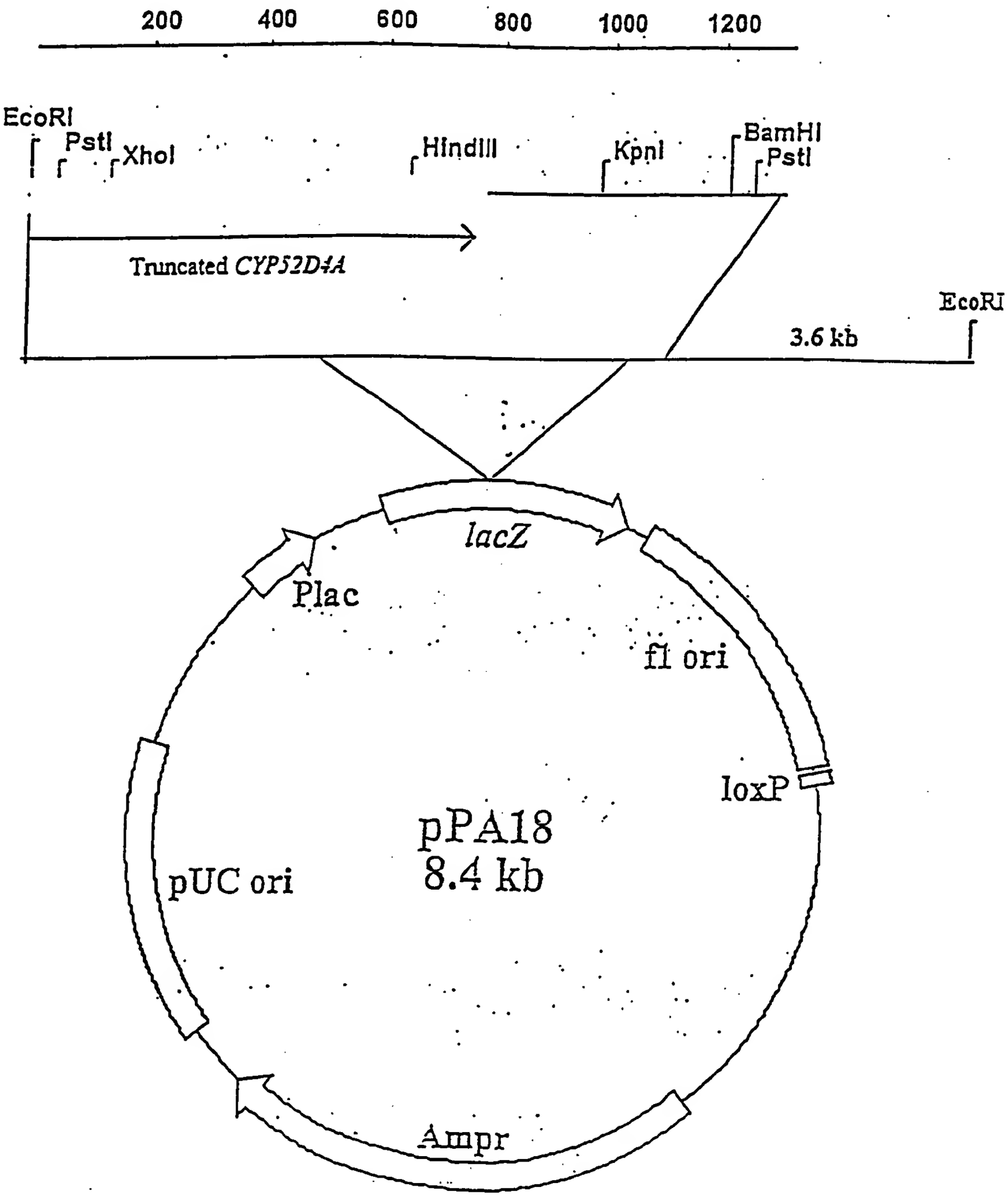
200
400
600
800
1000
1200
EcoRI
PstI
XhoI
HindIII
KpnI
BamHI
PstI
Truncated CYP52D4A
EcoRI
3.6 kb
lacZ
Plac
f1 ori
loxP
pPA18
8.4 kb
pUC ori
Ampr

Figure 33

Expression of CYP52A1, CYP52A2 and CYP52A5 in Henkel Fermentor Run 3538-98

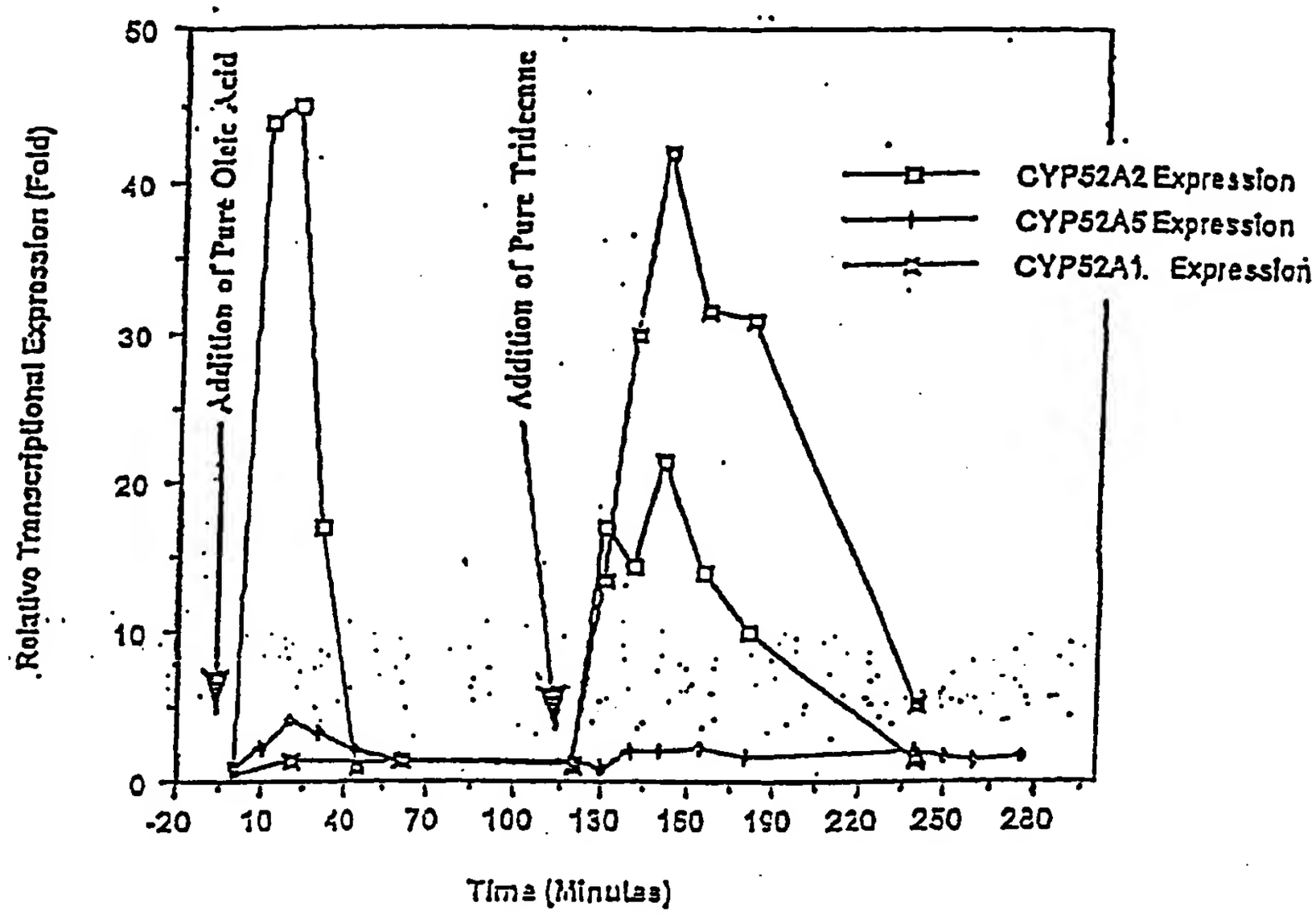

Figure 34

Figure 35

1 gram (g) Whole fermentation broth (70°C)
+
1g Internal standard C15:0 10g/l in 1N KOH (70°C)
+
0.8 ml 6N HCl
+
6 ml Methyl-t-Butyl-Ether (MtBE)

↓ extract in 60 ml separatory funnel

1 ml MtBE phase pipeted into 12X75mm test tube

↓

Dry down to solids under N_2 stream

↓

Add 1 ml 12% BF3-Methanol (Kodak, 4°C) and stopper test tube

↓

Dissolve solids, esterify for 15 min. @ 60°C, quiescently

↓

Add 0.25 ml saturated NaCl solution (71.5g NaCl/200ml H2O)

↓ Vortex to mix

Add 1 ml Mixed Ethers (50% diethyl ether 50% petroleum ether, v/v)

↓

Shake for 1 min. to extract methylesters

↓

Inject 5 ul of Mixed Ether phase into GC

<u>GC parameters</u>

Column : HP-INNOWAX capillary column, 30m X 0.32mm, 0.5µm film thickness
Split Ratio : 1:100
Column Head Pressure : 13.5 psig
Injector Temperature : 240°C
FID Detector Temp. : 250°C
Temp. Prog. : 90°C for 0 min. to 190°C @ 7°C/min. for 0 min. to 235°C @ 12°C/min. for 30 min.

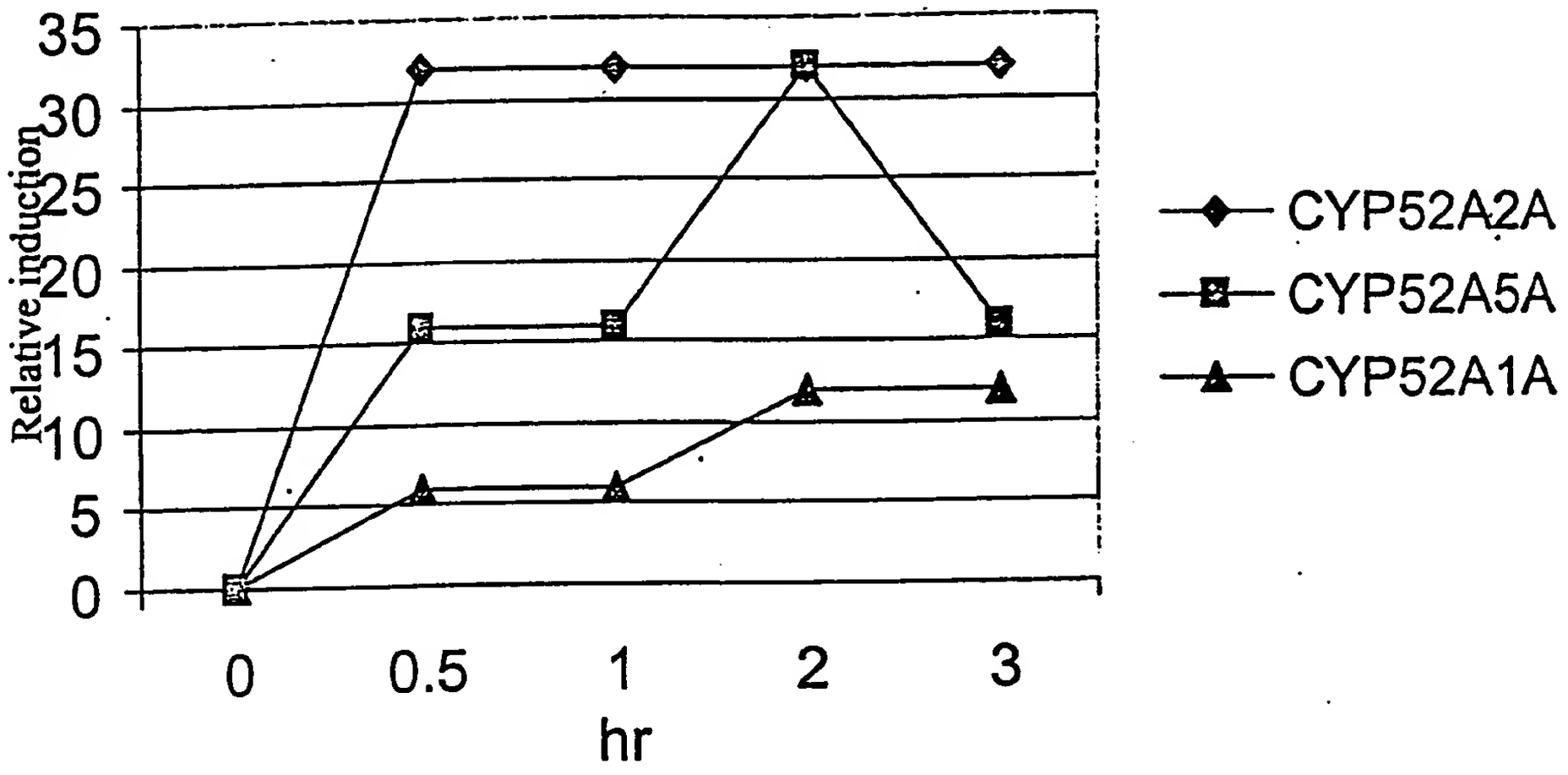
35
30
25
20
15
10
5
0
Relative induction
0
0.5
1
2
3
hr
CYP52A2A
CYP52A5A
CYP52A1A

Figure 36

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: Wilson, C. Ron
Craft, David L.
Eirich, Dudley
Eshoo, Mark
Madduri, Krishna M.
Cornett, Cathy A.
Brenner, Alfred A.
Tang, Maria
Loper, John C.
Gleeson, Martin

(ii) TITLE OF INVENTION: CYTOCHROME P450 MONOOXYGENASE AND NADPH CYTOCHROME P450 OXIDOREDUCTASE GENES AND PROTEINS RELATED TO THE OMEGA HYDROXYLASE COMPLEX OF *CANDIDA TROPICALIS* AND METHODS RELATING THERETO

(iii) NUMBER OF SEQUENCES: 107

(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: HENKEL CORPORATION
(B) STREET: 2500 Renaissance Boulevard, Suite 200
(C) CITY: Gulph Mills
(D) STATE: PA
(E) COUNTRY: U.S.A.
(F) ZIP: 19406

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30

(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:

(viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: Drach, John E.

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:
CCTTAATTAA ATGCACGAAG CGGAGATAAA AG 32

(2) INFORMATION FOR SEQ ID NO:2:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:
CCTTAATTAA GCATAAGCTT GCTCGAGTCT 30

(2) INFORMATION FOR SEQ ID NO:3:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:
CCTTAATTAA ACGCAATGGG AACATGGAGT G 31

(2) INFORMATION FOR SEQ ID NO:4:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 34 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:
CCTTAATTAA TCGCACTACG GTTATTGGTA TCAG 34

(2) INFORMATION FOR SEQ ID NO:5:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:
CCTTAATTAA TCAAAGTACG TTCAGGCGG 29

(2) INFORMATION FOR SEQ ID NO:6:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 34 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:
CCTTAATTAA GGCAGACAAC AACTTGGCAA AGTC 34

(2) INFORMATION FOR SEQ ID NO:7:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid

(2) INFORMATION FOR SEQ ID NO:13:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:
GGGTTTAAAC 10

(2) INFORMATION FOR SEQ ID NO:14:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:
AGGCGCGCC 9

(2) INFORMATION FOR SEQ ID NO:15:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:
CCTTAATTAA 10

(2) INFORMATION FOR SEQ ID NO:16:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 3..4
(D) OTHER INFORMATION: /note= "y=dCTP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 9..10
(D) OTHER INFORMATION: /note= "w=dATP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 15..16
(D) OTHER INFORMATION: /note= "w=dATP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 18..19
(D) OTHER INFORMATION: /note= "w=dATP or dTTP"
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:
TCYCAAACWG GTACWGCWGA A 21

(2) INFORMATION FOR SEQ ID NO:17:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 12..13
(D) OTHER INFORMATION: /note= "y=dCTP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 15..16
(D) OTHER INFORMATION: /note= "w=dATP or dTTP"
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:
GGTTTGGGTA AYTCWACTTA T 21

(2) INFORMATION FOR SEQ ID NO:18:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:
CGTTATTATC ATTTCTTC 18

(2) INFORMATION FOR SEQ ID NO:19:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 3..4
(D) OTHER INFORMATION: /note= "m=dATP or dCTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 9..10
(D) OTHER INFORMATION: /note= "r=dATP or dGTP"
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:
GCMACACCRGTA CCTGGACC 20

(2) INFORMATION FOR SEQ ID NO:20:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:
ATCCCAATCG TAATCAGC 18

(2) INFORMATION FOR SEQ ID NO:21:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:
ACTTGTCTTC GTTTAGCA 18

(2) INFORMATION FOR SEQ ID NO:22:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:
CTACGTCTGT GGTGATGC 18

(2) INFORMATION FOR SEQ ID NO:23:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 17 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 3..4
(D) OTHER INFORMATION: /note= "n=dATP or dCTP or dGTP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 6..7
(D) OTHER INFORMATION: /note= "Y=dCTP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 9..10
(D) OTHER INFORMATION: /note= "n=dATP or dCTP or dGTP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 12..13
(D) OTHER INFORMATION: /note= "n=dATP or dCTP or dGTP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 15..16
(D) OTHER INFORMATION: /note= "n=dATP or dCTP or dGTP or dTTP"
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:
CGNGAYACNAC NGCNGG 17

(2) INFORMATION FOR SEQ ID NO:24:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 17 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 3..4
(D) OTHER INFORMATION: /note= "r=dATP or dGTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 6..7
(D) OTHER INFORMATION: /note= "y=dCTP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 9..10
(D) OTHER INFORMATION: /note= "n=dATP or dCTP or dGTP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 12..13
(D) OTHER INFORMATION: /note= "n=dATP or dCTP or dGTP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 15..16
(D) OTHER INFORMATION: /note= "n=dATP or dCTP or dGTP or dTTP"
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:
AGRGAYACNA CNGCNGG 17

(2) INFORMATION FOR SEQ ID NO:25:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 17 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 3..4
(D) OTHER INFORMATION: /note= "n=dATP or dCTP or dGTP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 6..7
(D) OTHER INFORMATION: /note= "r=dATP or dGTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 9..10
(D) OTHER INFORMATION: /note= "y=dCTP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 12..13
(D) OTHER INFORMATION: /note= "y=dCTP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 15..16

(D) OTHER INFORMATION: /note= "n=dATP or dCTP or dGTP or dTTP"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

AGNGCRAAYT GYTGNCC 17

2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 18 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(ix) FEATURE:

(A) NAME/KEY: misc_feature

(B) LOCATION: 1..2

(D) OTHER INFORMATION: /note= "y=dCTP or dTTP"

(ix) FEATURE:

(A) NAME/KEY: misc_feature

(B) LOCATION: 4..5

(D) OTHER INFORMATION: /note= "n=dATP or dCTP or dGTP or dTTP"

(ix) FEATURE:

(A) NAME/KEY: misc_feature

(B) LOCATION: 7..8

(D) OTHER INFORMATION: /note= "r=dATP or dGTP"

(ix) FEATURE:

(A) NAME/KEY: misc_feature

(B) LOCATION: 10..11

(D) OTHER INFORMATION: /note= "y=dCTP or dTTP"

(ix) FEATURE:

(A) NAME/KEY: misc_feature

(B) LOCATION: 13..14

(D) OTHER INFORMATION: /note= "y=dCTP or dTTP"

(ix) FEATURE:

(A) NAME/KEY: misc_feature

(B) LOCATION: 16..17

(D) OTHER INFORMATION: /note= "n=dATP or dCTP or dGTP or dTTP"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

YAANGCRAAY TGYTGNCC 18

2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 29 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

ATTCAACGGT GGTCCAAGAA TCTGTTTGG 29

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 25 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:
GAGCTATGTT GAGACCACAG TTTGC 25

(2) INFORMATION FOR SEQ ID NO:29:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:
CTTCAGTTAA AGCAAATTGT TTGGCC 26

(2) INFORMATION FOR SEQ ID NO:30:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:
CTCGGGAAGC GCGCCATTGT GTTGG 25

2) INFORMATION FOR SEQ ID NO:31:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:
TAATACGACT CACTATAGGG CGAATTGGC 29

(2) INFORMATION FOR SEQ ID NO:32:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 3..4
(D) OTHER INFORMATION: /note= "r=dATP or dGTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 4..5
(D) OTHER INFORMATION: /note= "y=dCTP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 16..17
(D) OTHER INFORMATION: /note= "y=dCTP or dTTP"
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:
TGRYTCAAAC CATCTYTCTG G 21

(2) INFORMATION FOR SEQ ID NO:33:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 17 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:
GGACCGGCGT TAAAGGG 17

(2) INFORMATION FOR SEQ ID NO:34:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 9..10
(D) OTHER INFORMATION: /note= "w=dATP or dTTP"
(ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 12..13
(D) OTHER INFORMATION: /note= "y=dCTP or dTTP"
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:
CATAGTCGWA TYATGCTTAG ACC 23

2) INFORMATION FOR SEQ ID NO:35:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 17 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:
GGACCACCAT TGAATGG 17

(2) INFORMATION FOR SEQ ID NO:36:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 540 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA (genomic)
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

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ATGATTGAAC AACTCCTAGA ATATTGGTAT GTCGTTGTGC CAGTGTTGTA CATCATCAAA      60
CAACTCCTTG CATACACAAA GACTCGCGTC TTGATGAAAA AGTTGGGTGC TGCTCCAGTC     120
ACAAACAAGT TGTACGACAA CGCTTTCGGT ATCGTCAATG GATGGAAGGC TCTCCAGTTC     180
AAGAAAGAGG GCAGGGCTCA AGAGTACAAC GATTACAAGT TTGACCACTC CAAGAACCCA     240
AGCGTGGGCA CCTACGTCAG TATTCTTTTC GGCACCAGGA TCGTCGTGAC CAAAGATCCA     300
GAGAATATCA AAGCTATTTT GGCAACCCAG TTTGGTGATT TTTCTTTGGG CAAGAGGCAC     360
ACTCTTTTTA AGCCTTTGTT AGGTGATGGG ATCTTCACAT TGGACGGCGA AGGCTGGAAG     420
CACAGCAGAG CCATGTTGAG ACCACAGTTT GCCAGAGAAC AAGTTGCTCA TGTGACGTCG     480
TTGGAACCAC ACTTCCAGTT GTTGAAGAAG CATATTCTTA AGCACAAGGG TGAATACTTT     540
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2) INFORMATION FOR SEQ ID NO:37:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:
CCGATGAAGT TTTCGACGAG TACCC 25

2) INFORMATION FOR SEQ ID NO:38:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:
AAGGCTTTAA CGTGTCCAAT CTGGTC 26

(2) INFORMATION FOR SEQ ID NO:39:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:
ATTATCGCCA CATACTTCAC CAAATGG 27

(2) INFORMATION FOR SEQ ID NO:40:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:
CGAGATCGTG GATACGCTGG AGTG 24

(2) INFORMATION FOR SEQ ID NO:41:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:
GCCACTCGGT AACTTTGTCA GGGAC 25

(2) INFORMATION FOR SEQ ID NO:42:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:
CATTGAACTG AGTAGCCAAA ACAGCC 26

(2) INFORMATION FOR SEQ ID NO:43:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:
CCTACGTTTG GTATCGCTAC TCCGTTG 27

(2) INFORMATION FOR SEQ ID NO:44:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:
TTTCCAGCCA GCACCGTCCA AG 22

(2) INFORMATION FOR SEQ ID NO:45:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:
GCAGAGCCGA TCTATGTTGC GTCC 24

(2) INFORMATION FOR SEQ ID NO:46:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:
TCATTGAATG CTTCCAGGAA CCTCG 25

2) INFORMATION FOR SEQ ID NO:47:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:
AAGAGGGCAG GGCTCAAGAG 20

(2) INFORMATION FOR SEQ ID NO:48:
(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:
TCCATGTGAA GATCCCATCA C 21

(2) INFORMATION FOR SEQ ID NO:49:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:
CTTGAAGGCC GTGTTGAACG 20

(2) INFORMATION FOR SEQ ID NO:50:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:
CAGGATTTGT CTGAGTTGCC G 21

(2) INFORMATION FOR SEQ ID NO:51:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:
CCATTGCCTT GAGATACGCC ATTGGTAG 28

(2) INFORMATION FOR SEQ ID NO:52:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:
AGCCTTGGTG TCGTTCTTTT CAACGG 26

(2) INFORMATION FOR SEQ ID NO:53:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:
TTGGGTTTGT TTGTTTCCTG TGTCCG 26

(2) INFORMATION FOR SEQ ID NO:54:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:
CCTTTGACCT TCAATCTGGC GTAGACG 27

(2) INFORMATION FOR SEQ ID NO:55:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:
GTTTGCTGAA TACGCTGAAG GTGATG 26

(2) INFORMATION FOR SEQ ID NO:56:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:
TGGAGCTGAA CAACTCTCTC GTCTCGG 27

(2) INFORMATION FOR SEQ ID NO:57:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:
TTCCTCAACA CGGACAGCGG 20

2) INFORMATION FOR SEQ ID NO:58:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:
AGTCAACCAG GTGTGGAACT CGTC 24

(2) INFORMATION FOR SEQ ID NO:59:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 49 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:
GGATCCTAAT ACGACTCACT ATAGGGAGGA AGAGGGCAGG GCTCAAGAG 49

(2) INFORMATION FOR SEQ ID NO:60:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 42 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:
TCCATGTGAA GATCCCATCA CGAGTGTGCC TCTTGCCCAA AG 42

(2) INFORMATION FOR SEQ ID NO:61:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 54 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:
GGATCCTAAT ACGACTCACT ATAGGGAGGC CGATGAAGTT TTCGACGAGT ACCC 54

(2) INFORMATION FOR SEQ ID NO:62:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 52 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:
AAGGCTTTAA CGTGTCCAAT CTGGTCAACA TAGCTCTGGA GTGCTTCCAA CC 52

(2) INFORMATION FOR SEQ ID NO:63:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 56 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:
GGATCCTAAT ACGACTCACT ATAGGGAGGA TTATCGCCAC ATACTTCACC AAATGG 56

(2) INFORMATION FOR SEQ ID NO:64:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 52 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:
CGAGATCGTG GATACGCTGG AGTGCGTCGC TCTTCTTCTT CAACAATTCA AG 52

(2) INFORMATION FOR SEQ ID NO:65:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 49 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:
CATTGAACTG AGTAGCCAAA ACAGCCCATG GTTTCAATCA ATGGGAGGC 49

(2) INFORMATION FOR SEQ ID NO:66:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 54 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:
GGATCCTAAT ACGACTCACT ATAGGGAGGG CCACTCGGTA ACTTTGTCAG GGAC 54

(2) INFORMATION FOR SEQ ID NO:67:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 56 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:
GGATCCTAAT ACGACTCACT ATAGGGAGGC CTACGTTTGG TATCGCTACT CCGTTG 56

2) INFORMATION FOR SEQ ID NO:68:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 48 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:
TTTCCAGCCA GCACCGTCCA AGCAACAAGG AGTACAAGAA ATCGTGTC 48

(2) INFORMATION FOR SEQ ID NO:69:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 53 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:
GGATCCTAAT ACGACTCACT ATAGGGAGGG CAGAGCCGAT CTATGTTGCG TCC 53

(2) INFORMATION FOR SEQ ID NO:70:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 45 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:
TCATTGAATG CTTCCAGGAA CCTCGCCACA TCCATCGAGA ACCGG 45

(2) INFORMATION FOR SEQ ID NO:71:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 49 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:
GGATCCTAAT ACGACTCACT ATAGGGAGGC TTGAAGGCCG TGTTGAACG 49

(2) INFORMATION FOR SEQ ID NO:72:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 46 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:
CAGGATTTGT CTGAGTTGCC GCCTGATCAA GATAGGATCC TTGCCG 46

(2) INFORMATION FOR SEQ ID NO:73:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 56 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:
GGATCCTAAT ACGACTCACT ATAGGGAGGG GTTTGCTGAA TACGCTGAAG GTGATG 56

(2) INFORMATION FOR SEQ ID NO:74:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 52 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:
TGGAGCTGAA CAACTCTCTC GTCTCGGGTG GTCGAATGGA CCCTTGGTCA AG 52

(2) INFORMATION FOR SEQ ID NO:75:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 49 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:
GGATCCTAAT ACGACTCACT ATAGGGAGGT TCCTCAACAC GGACAGCGG 49

(2) INFORMATION FOR SEQ ID NO:76:
(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 49 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:
AGTCAACCAG GTGTGGAACT CGTCGGTGGC AACAATGAAA AACACCAAG 49

(2) INFORMATION FOR SEQ ID NO:77:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 57 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:
GGATCCTAAT ACGACTCACT ATAGGGAGGC CATTGCCTTG AGATACGCCA TTGGTAG 57

2) INFORMATION FOR SEQ ID NO:78:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 53 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:
AGCCTTGGTG TCGTTCTTTT CAACGGAAGG TGGTCTCGAT GGTGTGTTCA ACC 53

(2) INFORMATION FOR SEQ ID NO:79:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 55 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:
GGATCCTAAT ACGACTCACT ATAGGGAGGT TGGGTTTGTT TGTTTCCTGT GTCCG 55

(2) INFORMATION FOR SEQ ID NO:80:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 50 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:
CCTTTGACCT TCAATCTGGC GTAGACGCAG CACCACCGAT CCACCACTTG 50

(2) INFORMATION FOR SEQ ID NO:81:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 4206 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

CATCAAGATC ATCTATGGGG ATAATTACGA CAGCAACATT GCAGAAAGAG CGTTGGTCAC 60
AATCGAAAGA GCCTATGGCG TTGCCGTCGT TGAGGCAAAT GACAGCACCA ACAATAACGA 120
TGGTCCCAGT GAAGAGCCTT CAGAACAGTC CATTGTTGAC GCTTAAGGCA CGGATAATTA 180
CGTGGGGCAA AGGAACGCGG AATTAGTTAT GGGGGGATCA AAAGCGGAAG ATTTGTGTTG 240
CTTGTGGGTT TTTTCCTTTA TTTTTCATAT GATTTCTTTG CGCAAGTAAC ATGTGCCAAT 300
TTAGTTTGTG ATTAGCGTGC CCCACAATTG GCATCGTGGA CGGGCGTGTT TTGTCATACC 360
CCAAGTCTTA ACTAGCTCCA CAGTCTCGAC GGTGTCTCGA CGATGTCTTC TTCCACCCCT 420
CCCATGAATC ATTCAAAGTT GTTGGGGGAT CTCCACCAAG GGCACCGGAG TTAATGCTTA 480
TGTTTCTCCC ACTTTGGTTG TGATTGGGGT AGTCTAGTGA GTTGGAGATT TTCTTTTTTT 540
CGCAGGTGTC TCCGATATCG AAATTTGATG AATATAGAGA GAAGCCAGAT CAGCACAGTA 600
GATTGCCTTT GTAGTTAGAG ATGTTGAACA GCAACTAGTT GAATTACACG CCACCACTTG 660
ACAGCAAGTG CAGTGAGCTG TAAACGATGC AGCCAGAGTG TCACCACCAA CTGACGTTGG 720
GTGGAGTTGT TGTTGTTGTT GTTGGCAGGG CCATATTGCT AAACGAAGAC AAGTAGCACA 780
AAACCCAAGC TTAAGAACAA AAATAAAAAA AATTCATACG ACAATTCCAA AGCCATTGAT 840
TTACATAATC AACAGTAAGA CAGAAAAAAC TTTCAACATT TCAAAGTTCC CTTTTTCCTA 900
TTACTTCTTT TTTTTCTTCT TTCCTTCTTT CCTTCTGTTT TTCTTACTTT ATCAGTCTTT 960
TACTTGTTTT TGCAATTCCT CATCCTCCTC CTACTCCTCC TCACCATGGC TTTAGACAAG 1020
TTAGATTTGT ATGTCATCAT AACATTGGTG GTCGCTGTAG CCGCCTATTT TGCTAAGAAC 1080
CAGTTCCTTG ATCAGCCCCA GGACACCGGG TTCCTCAACA CGGACAGCGG AAGCAACTCC 1140
AGAGACGTCT TGCTGACATT GAAGAAGAAT AATAAAAACA CGTTGTTGTT GTTTGGGTCC 1200
CAGACGGGTA CGGCAGAAGA TTACGCCAAC AAATTGTCCA GAGAATTGCA CTCCAGATTT 1260
GGCTTGAAAA CGATGGTTGC AGATTTCGCT GATTACGATT GGGATAACTT CGGAGATATC 1320
ACCGAAGACA TCTTGGTGTT TTTCATTGTT GCCACCTATG GTGAGGGTGA ACCTACCGAT 1380
AATGCCGACG AGTTCCACAC CTGGTTGACT GAAGAAGCTG ACACTTTGAG TACCTTGAAA 1440
TACACCGTGT TCGGGTTGGG TAACTCCACG TACGAGTTCT TCAATGCCAT TGGTAGAAAG 1500
TTTGACAGAT TGTTGAGCGA GAAAGGTGGT GACAGGTTTG CTGAATACGC TGAAGGTGAT 1560
GACGGTACTG GCACCTTGGA CGAAGATTTC ATGGCCTGGA AGGACAATGT CTTTGACGCC 1620
TTGAAGAATG ATTTGAACTT TGAAGAAAAG GAATTGAAGT ACGAACCAAA CGTGAAATTG 1680
ACTGAGAGAG ACGACTTGTC TGCTGCTGAC TCCCAAGTTT CCTTGGGTGA GCCAAACAAG 1740
AAGTACATCA ACTCCGAGGG CATCGACTTG ACCAAGGGTC CATTCGACCA CACCCACCCA 1800
TACTTGGCCA GAATCACCGA GACGAGAGAG TTGTTCAGCT CCAAGGACAG ACACTGTATC 1860
CACGTTGAAT TTGACATTTC TGAATCGAAC TTGAAATACA CCACCGGTGA CCATCTAGCT 1920
ATCTGGCCAT CCAACTCCGA CGAAAACATT AAGCAATTTG CCAAGTGTTT CGGATTGGAA 1980
GATAAACTCG ACACTGTTAT TGAATTGAAG GCGTTGGACT CCACTTACAC CATCCCATTC 2040
CCAACCCCAA TTACCTACGG TGCTGTCATT AGACACCATT TAGAAATCTC CGGTCCAGTC 2100
TCGAGACAAT TCTTTTTGTC AATTGCTGGG TTTGCTCCTG ATGAAGAAAC AAAGAAGGCT 2160
TTTACCAGAC TTGGTGGTGA CAAGCAAGAA TTCGCCGCCA AGGTCACCCG CAGAAAGTTC 2220
AACATTGCCG ATGCCTTGTT ATATTCCTCC AACAACGCTC CATGGTCCGA TGTTCCTTTT 2280
GAATTCCTTA TTGAAAACGT TCCACACTTG ACTCCACGTT ACTACTCCAT TTCGTCTTCG 2340
TCATTGAGTG AAAAGCAACT CATCAACGTT ACTGCAGTTG TTGAAGCCGA AGAAGAAGCT 2400
GATGGCAGAC CAGTCACTGG TGTTGTCACC AACTTGTTGA AGAACGTTGA AATTGTGCAA 2460
AACAAGACTG GCGAAAAGCC ACTTGTCCAC TACGATTTGA GCGGCCCAAG AGGCAAGTTC 2520
AACAAGTTCA AGTTGCCAGT GCATGTGAGA AGATCCAACT TTAAGTTGCC AAAGAACTCC 2580
ACCACCCCAG TTATCTTGAT TGGTCCAGGT ACTGGTGTTG CCCCATTGAG AGGTTTTGTC 2640
AGAGAAAGAG TTCAACAAGT CAAGAATGGT GTCAATGTTG GCAAGACTTT GTTGTTTTAT 2700
GGTTGCAGAA ACTCCAACGA GGACTTTTTG TACAAGCAAG AATGGGCCGA GTACGCTTCT 2760
GTTTTGGGTG AAAACTTTGA GATGTTCAAT GCCTTCTCCA GACAAGACCC ATCCAAGAAG 2820
GTTTACGTCC AGGATAAGAT TTTAGAAAAC AGCCAACTTG TGCACGAGTT GTTGACTGAA 2880
GGTGCCATTA TCTACGTCTG TGGTGATGCC AGTAGAATGG CTAGAGACGT GCAGACCACA 2940
ATTTCCAAGA TTGTTGCTAA AAGCAGAGAA ATTAGTGAAG ACAAGGCTGC TGAATTGGTC 3000
AAGTCCTGGA AGGTCCAAAA TAGATACCAA GAAGATGTTT GGTAGACTCA AACGAATCTC 3060
TCTTTCTCCC AACGCATTTA TGAATCTTTA TTCTCATTGA AGCTTTACAT ATGTTCTACA 3120
CTTTATTTTT TTTTTTTTTT TTATTATTAT ATTACGAAAC ATAGGTCAAC TATATATACT 3180
TGATTAAATG TTATAGAAAC AATAACTATT ATCTACTCGT CTACTTCTTT GGCATTGACA 3240
TCAACATTAC CGTTCCCATT ACCGTTGCCG TTGGCAATGC CGGGATATTT AGTACAGTAT 3300

CTCCAATCCG GATTTGAGCT ATTGTAGATC AGCTGCAAGT CATTCTCCAC CTTCAACCAG 3360
TACTTATACT TCATCTTTGA CTTCAAGTCC AAGTCATAAA TATTACAAGT TAGCAAGAAC 3420
TTCTGGCCAT CCACGATATA GACGTTATTC ACGTTATTAT GCGACGTATG GATGTGGTTA 3480
TCCTTATTGA ACTTCTCAAA CTTCAAAAAC AACCCCACGT CCCGCAACGT CATTATCAAC 3540
GACAAGTTCT GGCTCACGTC GTCGGAGCTC GTCAAGTTCT CAATTAGATC GTTCTTGTTA 3600
TTGATCTTCT GGTACTTTCT CAATTGCTGG AACACATTGT CCTCGTTGTT CAAATAGATC 3660
TTGAACAACT TTTTCAACGG GATCAACTTC TCAATCTGGG CCAAGATCTC CGCCGGGATC 3720
TTCAGAAACA AGTCCTGCAA CCCCTGGTCG ATGGTCTCCG GGTACAACAA GTCCAAGGGG 3780
CAGAAGTGTC TAGGCACGTG TTTCAACTGG TTCAACGAAC ATGTTCGACA GTAGTTCGAG 3840
TTATAGTTAT CGTACAACCA TTTTGGTTTG ATTTCGAAAA TGACGGAGCT GATGCCATCA 3900
TTCTCCTGGT TCCTCTCATA GTACAACTGG CACTTCTTCG AGAGGCTCAA TTCCTCGTAG 3960
TTCCCGTCCA AGATATTCGG CAACAAGAGC CCGTACCGCT CACGGAGCAT CAAGTCGTGG 4020
CCCTGGTTGT TCAACTTGTT GATGAAGTCC GAGGTCAAGA CAATCAACTG GATGTCGATG 4080
ATCTGGTGCG GGAACAAGTT CTTGCATTTT AGCTCGATGA AGTCGTACAA CTCACACGTC 4140
GAGATATACT CCTGTTCCTC CTTCAAGAGC CGGATCCGCA AGAGCTTGTG CTTCAAGTAG 4200
TCGTTG 4206

(2) INFORMATION FOR SEQ ID NO:82:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 4145 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA (genomic)
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

TATATGATAT ATGATATATC TTCCTGTGTA ATTATTATTC GTATTCGTTA ATACTTACTA 60
CATTTTTTTT TCTTTATTTA TGAAGAAAAG GAGAGTTCGT AAGTTGAGTT GAGTAGAATA 120
GGCTGTTGTG CATACGGGGA GCAGAGGAGA GTATCCGACG AGGAGGAACT GGGTGAAATT 180
TCATCTATGC TGTTGCGTCC TGTACTGTAC TGTAAATCTT AGATTTCCTA GAGGTTGTTC 240
TAGCAAATAA AGTGTTTCAA GATACAATTT TACAGGCAAG GGTAAAGGAT CAACTGATTA 300
GCGGAAGATT GGTGTTGCCT GTGGGGTTCT TTTATTTTTC ATATGATTTC TTTGCGCGAG 360
TAACATGTGC CAATCTAGTT TATGATTAGC GTACCTCCAC AATTGGCATC TTGGACGGGC 420
GTGTTTTGTC TTACCCCAAG CCTTATTTAG TTCCACAGTC TCGACGGTGT CTCGCCGATG 480
TCTTCTCCCA CCCCTCGCAG GAATCATTCG AAGTTGTTGG GGGATCTCCT CCGCAGTTTA 540
TGTTCATGTC TTTCCCACTT TGGTTGTGAT TGGGGTAGCG TAGTGAGTTG GTGATTTTCT 600
TTTTTCGCAG GTGTCTCCGA TATCGAAGTT TGATGAATAT AGGAGCCAGA TCAGCATGGT 660
ATATTGCCTT TGTAGATAGA GATGTTGAAC AACAACTAGC TGAATTACAC ACCACCGCTA 720
AACGATGCGC ACAGGGTGTC ACCGCCAACT GACGTTGGGT GGAGTTGTTG TTGGCAGGGC 780
CATATTGCTA AACGAAGAGA AGTAGCACAA AACCCAAGGT TAAGAACAAT TAAAAAAATT 840
CATACGACAA TTCCACAGCC ATTTACATAA TCAACAGCGA CAAATGAGAC AGAAAAAACT 900
TTCAACATTT CAAAGTTCCC TTTTTCCTAT TACTTCTTTT TTTCTTTCCT TCCTTTCATT 960
TCCTTTCCTT CTGCTTTTAT TACTTTACCA GTCTTTTGCT TGTTTTTGCA ATTCCTCATC 1020
CTCCTCCTCA CCATGGCTTT AGACAAGTTA GATTTGTATG TCATCATAAC ATTGGTGGTC 1080
GCTGTGGCCG CCTATTTTGC TAAGAACCAG TTCCTTGATC AGCCCCAGGA CACCGGGTTC 1140
CTCAACACGG ACAGCGGAAG CAACTCCAGA GACGTCTTGC TGACATTGAA GAAGAATAAT 1200
AAAAACACGT TGTTGTTGTT TGGGTCCCAG ACCGGTACGG CAGAAGATTA CGCCAACAAA 1260
TTGTCAAGAG AATTGCACTC CAGATTTGGC TTGAAAACCA TGGTTGCAGA TTTCGCTGAT 1320
TACGATTGGG ATAACTTCGG AGATATCACC GAAGATATCT TGGTGTTTTT CATCGTTGCC 1380
ACCTACGGTG AGGGTGAACC TACCGACAAT GCCGACGAGT TCCACACCTG GTTGACTGAA 1440
GAAGCTGACA CTTTGAGTAC TTTGAGATAT ACCGTGTTCG GGTTGGGTAA CTCCACCTAC 1500
GAGTTCTTCA ATGCTATTGG TAGAAAGTTT GACAGATTGT TGAGTGAGAA AGGTGGTGAC 1560
AGATTTGCTG AATATGCTGA AGGTGACGAC GGCACTGGCA CCTTGGACGA AGATTTCATG 1620
GCCTGGAAGG ATAATGTCTT TGACGCCTTG AAGAATGACT TGAACTTTGA AGAAAAGGAA 1680
TTGAAGTACG AACCAAACGT GAAATTGACT GAGAGAGATG ACTTGTCTGC TGCCGACTCC 1740
CAAGTTTCCT TGGGTGAGCC AAACAAGAAG TACATCAACT CCGAGGGCAT CGACTTGACC 1800
AAGGGTCCAT TCGACCACAC CCACCCATAC TTGGCCAGGA TCACCGAGAC CAGAGAGTTG 1860

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TTCAGCTCCA AGGAAAGACA CTGTATTCAC GTTGAATTTG ACATTTCTGA ATCGAACTTG    1920
AAATACACCA CCGGTGACCA TCTAGCCATC TGGCCATCCA ACTCCGACGA AAACATCAAG    1980
CAATTTGCCA AGTGTTTCGG ATTGGAAGAT AAACTCGACA CTGTTATTGA ATTGAAGGCA    2040
TTGGACTCCA CTTACACCAT TCCATTCCCA ACTCCAATTA CTTACGGTGC TGTCATTAGA    2100
CACCATTTAG AAATCTCCGG TCCAGTCTCG AGACAATTCT TTTTGTCGAT TGCTGGGTTT    2160
GCTCCTGATG AAGAAACAAA GAAGACTTTC ACCAGACTTG GTGGTGACAA ACAAGAATTC    2220
GCCACCAAGG TTACCCGCAG AAAGTTCAAC ATTGCCGATG CCTTGTTATA TTCCTCCAAC    2280
AACACTCCAT GGTCCGATGT TCCTTTTGAG TTCCTTATTG AAAACATCCA ACACTTGACT    2340
CCACGTTACT ACTCCATTTC TTCTTCGTCG TTGAGTGAAA AACAACTCAT CAATGTTACT    2400
GCAGTCGTTG AGGCCGAAGA AGAAGCCGAT GGCAGACCAG TCACTGGTGT TGTTACCAAC    2460
TTGTTGAAGA ACATTGAAAT TGCGCAAAAC AAGACTGGCG AAAAGCCACT TGTTCACTAC    2520
GATTTGAGCG GCCCAAGAGG CAAGTTCAAC AAGTTCAAGT TGCCAGTGCA CGTGAGAAGA    2580
TCCAACTTTA AGTTGCCAAA GAACTCCACC ACCCCAGTTA TCTTGATTGG TCCAGGTACT    2640
GGTGTTGCCC CATTGAGAGG TTTCGTTAGA GAAAGAGTTC AACAAGTCAA GAATGGTGTC    2700
AATGTTGGCA AGACTTTGTT GTTTTATGGT TGCAGAAACT CCAACGAGGA CTTTTTGTAC    2760
AAGCAAGAAT GGGCCGAGTA CGCTTCTGTT TTGGGTGAAA ACTTTGAGAT GTTCAATGCC    2820
TTCTCTAGAC AAGACCCATC CAAGAAGGTT TACGTCCAGG ATAAGATTTT AGAAAACAGC    2880
CAACTTGTGC ACGAATTGTT GACCGAAGGT GCCATTATCT ACGTCTGTGG TGACGCCAGT    2940
AGAATGGCCA GAGACGTCCA GACCACGATC TCCAAGATTG TTGCCAAAAG CAGAGAAATC    3000
AGTGAAGACA AGGCCGCTGA ATTGGTCAAG TCCTGGAAAG TCCAAAATAG ATACCAAGAA    3060
GATGTTTGGT AGACTCAAAC GAATCTCTCT TTCTCCCAAC GCATTTATGA ATATTCTCAT    3120
TGAAGTTTTA CATATGTTCT ATATTTCATT TTTTTTTTAT TATATTACGA AACATAGGTC    3180
AACTATATAT ACTTGATTAA ATGTTATAGA AACAATAATT ATTATCTACT CGTCTACTTC    3240
TTTGGCATTG GCATTGGCAT TGGCATTGGC ATTGCCGTTG CCGTTGGTAA TGCCGGGATA    3300
TTTAGTACAG TATCTCCAAT CCGGATTTGA GCTATTGTAA ATCAGCTGCA AGTCATTCTC    3360
CACCTTCAAC CAGTACTTAT ACTTCATCTT TGACTTCAAG TCCAAGTCAT AAATATTACA    3420
AGTTAGCAAG AACTTCTGGC CATCCACAAT ATAGACGTTA TTCACGTTAT TATGCGACGT    3480
ATGGATATGG TTATCCTTAT TGAACTTCTC AAACTTCAAA AACAACCCCA CGTCCCGCAA    3540
CGTCATTATC AACGACAAGT TCTGACTCAC GTCGTCGGAG CTCGTCAAGT TCTCAATTAG    3600
ATCGTTCTTG TTATTGATCT TCTGGTACTT TCTCAACTGC TGGAACACAT TGTCCTCGTT    3660
GTTCAAATAG ATCTTGAACA ACTTCTTCAA GGGAATCAAC TTTTCGATCT GGGCCAAGAT    3720
TTCCGCCGGG ATCTTCAGAA ACAAGTCCTG CAACCCCTGG TCGATGGTCT CGGGGTACAA    3780
CAAGTCTAAG GGGCAGAAGT GTCTAGGCAC GTGTTTCAAC TGGTTCAAGG AACATGTTCG    3840
ACAGTAGTTC GAGTTATAGT TATCGTACAA CCACTTTGGC TTGATTTCGA AAATGACGGA    3900
GCTGATCCCA TCATTCTCCT GGTTCCTTTC ATAGTACAAC TGGCATTTCT TCGAGAGACT    3960
CAACTCCTCG TAGTTCCCGT CCAAGATATT CGGCAACAAG AGCCCGTAGC GCTCACGGAG    4020
CATCAAGTCG TGGCCCTGGT TGTTCAACTT GTTGATGAAG TCCGATGTCA AGACAATCAA    4080
CTGGATGTCG ATGATCTGGT GCGGAAACAA GTTCTTGCAC TTTAGCTCGA TGAAGTCGTA    4140
CAACT                                                               4145
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(2) INFORMATION FOR SEQ ID NO:83:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 679 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

```
Met Ala Leu Asp Lys Leu Asp Leu Tyr Val Ile Ile Thr Leu Val Val
1               5                  10                  15
Ala Val Ala Ala Tyr Phe Ala Lys Asn Gln Phe Leu Asp Gln Pro Gln
            20                  25                  30
Asp Thr Gly Phe Leu Asn Thr Asp Ser Gly Ser Asn Ser Arg Asp Val
        35                  40                  45
Leu Leu Thr Leu Lys Lys Asn Asn Lys Asn Thr Leu Leu Leu Phe Gly
    50                  55                  60
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Ser Gln Thr Gly Thr Ala Glu Asp Tyr Ala Asn Lys Leu Ser Arg Glu
65                  70                  75                  80
Leu His Ser Arg Phe Gly Leu Lys Thr Met Val Ala Asp Phe Ala Asp
                85                  90                  95
Tyr Asp Trp Asp Asn Phe Gly Asp Ile Thr Glu Asp Ile Leu Val Phe
            100                 105                 110
Phe Ile Val Ala Thr Tyr Gly Glu Gly Glu Pro Thr Asp Asn Ala Asp
        115                 120                 125
Glu Phe His Thr Trp Leu Thr Glu Glu Ala Asp Thr Leu Ser Thr Leu
    130                 135                 140
Lys Tyr Thr Val Phe Gly Leu Gly Asn Ser Thr Tyr Glu Phe Phe Asn
145                 150                 155                 160
Ala Ile Gly Arg Lys Phe Asp Arg Leu Leu Ser Glu Lys Gly Gly Asp
                165                 170                 175
Arg Phe Ala Glu Tyr Ala Glu Gly Asp Asp Gly Thr Gly Thr Leu Asp
            180                 185                 190
Glu Asp Phe Met Ala Trp Lys Asp Asn Val Phe Asp Ala Leu Lys Asn
        195                 200                 205
Asp Leu Asn Phe Glu Glu Lys Glu Leu Lys Tyr Glu Pro Asn Val Lys
    210                 215                 220
Leu Thr Glu Arg Asp Asp Leu Ser Ala Ala Asp Ser Gln Val Ser Leu
225                 230                 235                 240
Gly Glu Pro Asn Lys Lys Tyr Ile Asn Ser Glu Gly Ile Asp Leu Thr
                245                 250                 255
Lys Gly Pro Phe Asp His Thr His Pro Tyr Leu Ala Arg Ile Thr Glu
            260                 265                 270
Thr Arg Glu Leu Phe Ser Ser Lys Asp Arg His Cys Ile His Val Glu
        275                 280                 285
Phe Asp Ile Ser Glu Ser Asn Leu Lys Tyr Thr Thr Gly Asp His Leu
    290                 295                 300
Ala Ile Trp Pro Ser Asn Ser Asp Glu Asn Ile Lys Gln Phe Ala Lys
305                 310                 315                 320
Cys Phe Gly Leu Glu Asp Lys Leu Asp Thr Val Ile Glu Leu Lys Ala
                325                 330                 335
Leu Asp Ser Thr Tyr Thr Ile Pro Phe Pro Thr Pro Ile Thr Tyr Gly
            340                 345                 350
Ala Val Ile Arg His His Leu Glu Ile Ser Gly Pro Val Ser Arg Gln
        355                 360                 365
Phe Phe Leu Ser Ile Ala Gly Phe Ala Pro Asp Glu Glu Thr Lys Lys
    370                 375                 380
Ala Phe Thr Arg Leu Gly Gly Asp Lys Gln Glu Phe Ala Ala Lys Val
385                 390                 395                 400
Thr Arg Arg Lys Phe Asn Ile Ala Asp Ala Leu Leu Tyr Ser Ser Asn
                405                 410                 415
Asn Ala Pro Trp Ser Asp Val Pro Phe Glu Phe Leu Ile Glu Asn Val
            420                 425                 430
Pro His Leu Thr Pro Arg Tyr Tyr Ser Ile Ser Ser Ser Ser Leu Ser
        435                 440                 445
Glu Lys Gln Leu Ile Asn Val Thr Ala Val Val Glu Ala Glu Glu Glu
    450                 455                 460
Ala Asp Gly Arg Pro Val Thr Gly Val Val Thr Asn Leu Leu Lys Asn
465                 470                 475                 480
Val Glu Ile Val Gln Asn Lys Thr Gly Glu Lys Pro Leu Val His Tyr
                485                 490                 495
Asp Leu Ser Gly Pro Arg Gly Lys Phe Asn Lys Phe Lys Leu Pro Val
            500                 505                 510
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His Val Arg Arg Ser Asn Phe Lys Leu Pro Lys Asn Ser Thr Thr Pro
515 520 525
Val Ile Leu Ile Gly Pro Gly Thr Gly Val Ala Pro Leu Arg Gly Phe
530 535 540
Val Arg Glu Arg Val Gln Gln Val Lys Asn Gly Val Asn Val Gly Lys
545 550 555 560
Thr Leu Leu Phe Tyr Gly Cys Arg Asn Ser Asn Glu Asp Phe Leu Tyr
565 570 575
Lys Gln Glu Trp Ala Glu Tyr Ala Ser Val Leu Gly Glu Asn Phe Glu
580 585 590
Met Phe Asn Ala Phe Ser Arg Gln Asp Pro Ser Lys Lys Val Tyr Val
595 600 605
Gln Asp Lys Ile Leu Glu Asn Ser Gln Leu Val His Glu Leu Leu Thr
610 615 620
Glu Gly Ala Ile Ile Tyr Val Cys Gly Asp Ala Ser Arg Met Ala Arg
625 630 635 640
Asp Val Gln Thr Thr Ile Ser Lys Ile Val Ala Lys Ser Arg Glu Ile
645 650 655
Ser Glu Asp Lys Ala Ala Glu Leu Val Lys Ser Trp Lys Val Gln Asn
660 665 670
Arg Tyr Gln Glu Asp Val Trp
675

(2) INFORMATION FOR SEQ ID NO:84:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 679 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: unknown
(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:
Met Ala Leu Asp Lys Leu Asp Leu Tyr Val Ile Ile Thr Leu Val Val
1 5 10 15
Ala Val Ala Ala Tyr Phe Ala Lys Asn Gln Phe Leu Asp Gln Pro Gln
20 25 30
Asp Thr Gly Phe Leu Asn Thr Asp Ser Gly Ser Asn Ser Arg Asp Val
35 40 45
Leu Leu Thr Leu Lys Lys Asn Asn Lys Asn Thr Leu Leu Leu Phe Gly
50 55 60
Ser Gln Thr Gly Thr Ala Glu Asp Tyr Ala Asn Lys Leu Ser Arg Glu
65 70 75 80
Leu His Ser Arg Phe Gly Leu Lys Thr Met Val Ala Asp Phe Ala Asp
85 90 95
Tyr Asp Trp Asp Asn Phe Gly Asp Ile Thr Glu Asp Ile Leu Val Phe
100 105 110
Phe Ile Val Ala Thr Tyr Gly Glu Gly Glu Pro Thr Asp Asn Ala Asp
115 120 125
Glu Phe His Thr Trp Leu Thr Glu Glu Ala Asp Thr Leu Ser Thr Leu
130 135 140
Arg Tyr Thr Val Phe Gly Leu Gly Asn Ser Thr Tyr Glu Phe Phe Asn
145 150 155 160
Ala Ile Gly Arg Lys Phe Asp Arg Leu Leu Ser Glu Lys Gly Gly Asp
165 170 175
Arg Phe Ala Glu Tyr Ala Glu Gly Asp Asp Gly Thr Gly Thr Leu Asp
180 185 190

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Glu Asp Phe Met Ala Trp Lys Asp Asn Val Phe Asp Ala Leu Lys Asn
        195                 200                 205
Asp Leu Asn Phe Glu Glu Lys Glu Leu Lys Tyr Glu Pro Asn Val Lys
    210                 215                 220
Leu Thr Glu Arg Asp Asp Leu Ser Ala Ala Asp Ser Gln Val Ser Leu
225                 230                 235                 240
Gly Glu Pro Asn Lys Lys Tyr Ile Asn Ser Glu Gly Ile Asp Leu Thr
                245                 250                 255
Lys Gly Pro Phe Asp His Thr His Pro Tyr Leu Ala Arg Ile Thr Glu
            260                 265                 270
Thr Arg Glu Leu Phe Ser Ser Lys Glu Arg His Cys Ile His Val Glu
        275                 280                 285
Phe Asp Ile Ser Glu Ser Asn Leu Lys Tyr Thr Thr Gly Asp His Leu
    290                 295                 300
Ala Ile Trp Pro Ser Asn Ser Asp Glu Asn Ile Lys Gln Phe Ala Lys
305                 310                 315                 320
Cys Phe Gly Leu Glu Asp Lys Leu Asp Thr Val Ile Glu Leu Lys Ala
                325                 330                 335
Leu Asp Ser Thr Tyr Thr Ile Pro Phe Pro Thr Pro Ile Thr Tyr Gly
            340                 345                 350
Ala Val Ile Arg His His Leu Glu Ile Ser Gly Pro Val Ser Arg Gln
        355                 360                 365
Phe Phe Leu Ser Ile Ala Gly Phe Ala Pro Asp Glu Glu Thr Lys Lys
    370                 375                 380
Thr Phe Thr Arg Leu Gly Gly Asp Lys Gln Glu Phe Ala Thr Lys Val
385                 390                 395                 400
Thr Arg Arg Lys Phe Asn Ile Ala Asp Ala Leu Leu Tyr Ser Ser Asn
                405                 410                 415
Asn Thr Pro Trp Ser Asp Val Pro Phe Glu Phe Leu Ile Glu Asn Ile
            420                 425                 430
Gln His Leu Thr Pro Arg Tyr Tyr Ser Ile Ser Ser Ser Ser Leu Ser
        435                 440                 445
Glu Lys Gln Leu Ile Asn Val Thr Ala Val Val Glu Ala Glu Glu Glu
    450                 455                 460
Ala Asp Gly Arg Pro Val Thr Gly Val Val Thr Asn Leu Leu Lys Asn
465                 470                 475                 480
Ile Glu Ile Ala Gln Asn Lys Thr Gly Glu Lys Pro Leu Val His Tyr
                485                 490                 495
Asp Leu Ser Gly Pro Arg Gly Lys Phe Asn Lys Phe Lys Leu Pro Val
            500                 505                 510
His Val Arg Arg Ser Asn Phe Lys Leu Pro Lys Asn Ser Thr Thr Pro
        515                 520                 525
Val Ile Leu Ile Gly Pro Gly Thr Gly Val Ala Pro Leu Arg Gly Phe
    530                 535                 540
Val Arg Glu Arg Val Gln Gln Val Lys Asn Gly Val Asn Val Gly Lys
545                 550                 555                 560
Thr Leu Leu Phe Tyr Gly Cys Arg Asn Ser Asn Glu Asp Phe Leu Tyr
                565                 570                 575
Lys Gln Glu Trp Ala Glu Tyr Ala Ser Val Leu Gly Glu Asn Phe Glu
            580                 585                 590
Met Phe Asn Ala Phe Ser Arg Gln Asp Pro Ser Lys Lys Val Tyr Val
        595                 600                 605
Gln Asp Lys Ile Leu Glu Asn Ser Gln Leu Val His Glu Leu Leu Thr
    610                 615                 620
Glu Gly Ala Ile Ile Tyr Val Cys Gly Asp Ala Ser Arg Met Ala Arg
625                 630                 635                 640
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Asp Val Gln Thr Thr Ile Ser Lys Ile Val Ala Lys Ser Arg Glu Ile
645 650 655
Ser Glu Asp Lys Ala Ala Glu Leu Val Lys Ser Trp Lys Val Gln Asn
660 665 670
Arg Tyr Gln Glu Asp Val Trp
675

(2) INFORMATION FOR SEQ ID NO:85:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 4115 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA (genomic)
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

CATATGCGCT AATCTTCTTT TTCTTTTTAT CACAGGAGAA ACTATCCCAC CCCCACTTCG 60
AAACACAATG ACAACTCCTG CGTAACTTGC AAATTCTTGT CTGACTAATT GAAAACTCCG 120
GACGAGTCAG ACCTCCAGTC AAACGGACAG ACAGACAAAC ACTTGGTGCG ATGTTCATAC 180
CTACAGACAT GTCAACGGGT GTTAGACGAC GGTTTCTTGC AAAGACAGGT GTTGGCATCT 240
CGTACGATGG CAACTGCAGG AGGTGTCGAC TTCTCCTTTA GGCAATAGAA AAAGACTAAG 300
AGAACAGCGT TTTTACAGGT TGCATTGGTT AATGTAGTAT TTTTTTAGTC CCAGCATTCT 360
GTGGGTTGCT CTGGGTTTCT AGAATAGGAA ATCACAGGAG AATGCAAATT CAGATGGAAG 420
AACAAAGAGA TAAAAAACAA AAAAAAACTG AGTTTTGCAC CAATAGAATG TTTGATGATA 480
TCATCCACTC GCTAAACGAA TCATGTGGGT GATCTTCTCT TTAGTTTTGG TCTATCATAA 540
AACACATGAA AGTGAAATCC AAATACACTA CACTCCGGGT ATTGTCCTTC GTTTTACAGA 600
TGTCTCATTG TCTTACTTTT GAGGTCATAG GAGTTGCCTG TGAGAGATCA CAGAGATTAT 660
CACACTCACA TTTATCGTAG TTTCCTATCT CATGCTGTGT GTCTCTGGTT GGTTCATGAG 720
TTTGGATTGT TGTACATTAA AGGAATCGCT GGAAAGCAAA GCTAACTAAA TTTTCTTTGT 780
CACAGGTACA CTAACCTGTA AAACTTCACT GCCACGCCAG TCTTTCCTGA TTGGGCAAGT 840
GCACAAACTA CAACCTGCAA AACAGCACTC CGCTTGTCAC AGGTTGTCTC CTCTCAACCA 900
ACAAAAAAAT AAGATTAAAC TTTCTTTGCT CATGCATCAA TCGGAGTTAT CTCTGAAAGA 960
GTTGCCTTTG TGTAATGTGT GCCAAACTCA AACTGCAAAA CTAACCACAG AATGATTTCC 1020
CTCACAATTA TATAAACTCA CCCACATTTC CACAGACCGT AATTTCATGT CTCACTTTCT 1080
CTTTTGCTCT TCTTTTACTT AGTCAGGTTT GATAACTTCC TTTTTTATTA CCCTATCTTA 1140
TTTATTTATT TATTCATTTA TACCAACCAA CCAACCATGG CCACACAAGA AATCATCGAT 1200
TCTGTACTTC CGTACTTGAC CAAATGGTAC ACTGTGATTA CTGCAGCAGT ATTAGTCTTC 1260
CTTATCTCCA CAAACATCAA GAACTACGTC AAGGCAAAGA AATTGAAATG TGTCGATCCA 1320
CCATACTTGA AGGATGCCGG TCTCACTGGT ATTCTGTCTT TGATCGCCGC CATCAAGGCC 1380
AAGAACGACG GTAGATTGGC TAACTTTGCC GATGAAGTTT TCGACGAGTA CCCAAACCAC 1440
ACCTTCTACT TGTCTGTTGC CGGTGCTTTG AAGATTGTCA TGACTGTTGA CCCAGAAAAC 1500
ATCAAGGCTG TCTTGGCCAC CCAATTCACT GACTTCTCCT TGGGTACCAG ACACGCCCAC 1560
TTTGCTCCTT TGTTGGGTGA CGGTATCTTC ACCTTGGACG GAGAAGGTTG GAAGCACTCC 1620
AGAGCTATGT TGAGACCACA GTTTGCTAGA GACCAGATTG GACACGTTAA AGCCTTGGAA 1680
CCACACATCC AAATCATGGC TAAGCAGATC AAGTTGAACC AGGGAAAGAC TTTCGATATC 1740
CAAGAATTGT TCTTTAGATT TACCGTCGAC ACCGCTACTG AGTTCTTGTT TGGTGAATCC 1800
GTTCACTCCT TGTACGATGA AAAATTGGGC ATCCCAACTC CAAACGAAAT CCCAGGAAGA 1860
GAAAACTTTG CCGCTGCTTT CAACGTTTCC CAACACTACT TGGCCACCAG AAGTTACTCC 1920
CAGACTTTTT ACTTTTTGAC CAACCCTAAG GAATTCAGAG ACTGTAACGC CAAGGTCCAC 1980
CACTTGGCCA AGTACTTTGT CAACAAGGCC TTGAACTTTA CTCCTGAAGA ACTCGAAGAG 2040
AAATCCAAGT CCGGTTACGT TTTCTTGTAC GAATTGGTTA AGCAAACCAG AGATCCAAAG 2100
GTCTTGCAAG ATCAATTGTT GAACATTATG GTTGCCGGAA GAGACACCAC TGCCGGTTTG 2160
TTGTCCTTTG CTTTGTTTGA ATTGGCTAGA CACCCAGAGA TGTGGTCCAA GTTGAGAGAA 2220
GAAATCGAAG TTAACTTTGG TGTTGGTGAA GACTCCCGCG TTGAAGAAAT TACCTTCGAA 2280
GCCTTGAAGA GATGTGAATA CTTGAAGGCT ATCCTTAACG AAACCTTGCG TATGTACCCA 2340
TCTGTTCCTG TCAACTTTAG AACCGCCACC AGAGACACCA CTTTGCCAAG AGGTGGTGGT 2400
GCTAACGGTA CCGACCCAAT CTACATTCCT AAAGGCTCCA CTGTTGCTTA CGTTGTCTAC 2460

AAGACCCACC GTTTGGAAGA ATACTACGGT AAGGACGCTA ACGACTTCAG ACCAGAAAGA 2520
TGGTTTGAAC CATCTACTAA GAAGTTGGGC TGGGCTTATG TTCCATTCAA CGGTGGTCCA 2580
AGAGTCTGCT TGGGTCAACA ATTCGCCTTG ACTGAAGCTT CTTATGTGAT CACTAGATTG 2640
GCCCAGATGT TTGAAACTGT CTCATCTGAT CCAGGTCTCG AATACCCTCC ACCAAAGTGT 2700
ATTCACTTGA CCATGAGTCA CAACGATGGT GTCTTTGTCA AGATGTAAAG TAGTCGATGC 2760
TGGGTATTCG ATTACATGTG TATAGGAAGA TTTTGGTTTT TTATTCGTTC TTTTTTTTAA 2820
TTTTTGTTAA ATTAGTTTAG AGATTTCATT AATACATAGA TGGGTGCTAT TTCCGAAACT 2880
TTACTTCTAT CCCCTGTATC CCTTATTATC CCTCTCAGTC ACATGATTGC TGTAATTGTC 2940
GTGCAGGACA CAAACTCCCT AACGGACTTA AACCATAAAC AAGCTCAGAA CCATAAGCCG 3000
ACATCACTCC TTCTTCTCTC TTCTCCAACC AATAGCATGG ACAGACCCAC CCTCCTATCC 3060
GAATCGAAGA CCCTTATTGA CTCCATACCC ACCTGGAAGC CCCTCAAGCC ACACACGTCA 3120
TCCAGCCCAC CCATCACCAC ATCCCTCTAC TCGACAACGT CCAAAGACGG CGAGTTCTGG 3180
TGTGCCCGGA AATCAGCCAT CCCGGCCACA TACAAGCAGC CGTTGATTGC GTGCATACTC 3240
GGCGAGCCCA CAATGGGAGC CACGCATTCG GACCATGAAG CAAAGTACAT TCACGAGATC 3300
ACGGGTGTTT CAGTGTCGCA GATTGAGAAG TTCGACGATG GATGGAAGTA CGATCTCGTT 3360
GCGGATTACG ACTTCGGTGG GTTGTTATCT AAACGAAGAT TCTATGAGAC GCAGCATGTG 3420
TTTCGGTTCG AGGATTGTGC GTACGTCATG AGTGTGCCTT TTGATGGACC CAAGGAGGAA 3480
GGTTACGTGG TTGGGACGTA CAGATCCATT GAAAGGTTGA GCTGGGGTAA AGACGGGGAC 3540
GTGGAGTGGA CCATGGCGAC GACGTCGGAT CCTGGTGGGT TTATCCCGCA ATGGATAACT 3600
CGATTGAGCA TCCCTGGAGC AATCGCAAAA GATGTGCCTA GTGTATTAAA CTACATACAG 3660
AAATAAAAAC GTGTCTTGAT TCATTGGTTT GGTTCTTGTT GGGTTCCGAG CCAATATTTC 3720
ACATCATCTC CTAAATTCTC CAAGAATCCC AACGTAGCGT AGTCCAGCAC GCCCTCTGAG 3780
ATCTTATTTA ATATCGACTT CTCAACCACC GGTGGAATCC CGTTCAGACC ATTGTTACCT 3840
GTAGTGTGTT TGCTCTTGTT CTTGATGACA ATGATGTATT TGTCACGATA CCTGAAATAA 3900
TAAAACATCC AGTCATTGAG CTTATTACTC GTGAACTTAT GAAAGAACTC ATTCAAGCCG 3960
TTCCCAAAAA ACCCAGAATT GAAGATCTTG CTCAACTGGT CATGCAAGTA GTAGATCGCC 4020
ATGATCTGAT ACTTTACCAA GCTATCCTCT CCAAGTTCTC CCACGTACGG CAAGTACGGC 4080
AACGAGCTCT GGAAGCTTTG TTGTTTGGGG TCATA 4115

(2) INFORMATION FOR SEQ ID NO:86:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3948 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA (genomic)
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

GACCTGTGAC GCTTCCGGTG TCTTGCCACC AGTCTCCAAG TTGACCGACG CCCAAGTCAT 60
GTACCACTTT ATTTCCGGTT ACACTTCCAA GATGGCTGGT ACTGAAGAAG GTGTCACGGA 120
ACCACAAGCT ACTTTCTCCG CTTGTTTCGG TCAACCATTC TTGGTGTTGC ACCCAATGAA 180
GTACGCTCAA CAATTGTCTG ACAAGATCTC GCAACACAAG GCTAACGCCT GGTTGTTGAA 240
CACCGGTTGG GTTGGTTCTT CTGCTGCTAG AGGTGGTAAG AGATGCTCAT TGAAGTACAC 300
CAGAGCCATT TTGGACGCTA TCCACTCTGG TGAATTGTCC AAGGTTGAAT ACGAAACTTT 360
CCCAGTCTTC AACTTGAATG TCCCAACCTC CTGTCCAGGT GTCCCAAGTG AAATCTTGAA 420
CCCAACCAAG GCCTGGACCG GAAGGTGTTG ACTCCTTCAA CAAGGAAATC AAGTCTTTGG 480
CTGGTAAGTT TGCTGAAAAC TTCAAGACCT ATGCTGACCA AGCTACCGCT GAAGTGAGAG 540
CTGCAGGTCC AGAAGCTTAA AGATATTTAT TCATTATTTA GTTTGCCTAT TTATTTCTCA 600
TTACCCATCA TCATTCAACA CTATATATAA AGTTACTTCG GATATCATTG TAATCGTGCG 660
TGTCGCAATT GGATGATTTG GAACTGCGCT TGAAACGGAT TCATGCACGA AGCGGAGATA 720
AAAGATTACG TAATTTATCT CCTGAGACAA TTTTAGCCGT GTTCACACGC CCTTCTTTGT 780
TCTGAGCGAA GGATAAATAA TTAGACTTCC ACAGCTCATT CTAATTTCCG TCACGCGAAT 840
ATTGAAGGGG GGTACATGTG GCCGCTGAAT GTGGGGGCAG TAAACGCAGT CTCTCCTCTC 900
CCAGGAATAG TGCAACGGAG GAAGGATAAC GGATAGAAAG CGGAATGCGA GGAAAATTTT 960
GAACGCGCAA GAAAAGCAAT ATCCGGGCTA CCAGGTTTTG AGCCAGGGAA CACACTCCTA 1020
TTTCTGCTCA ATGACTGAAC ATAGAAAAAA CACCAAGACG CAATGAAACG CACATGGACA 1080
TTTAGACCTC CCCACATGTG ATAGTTTGTC TTAACAGAAA AGTATAATAA GAACCCATGC 1140

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CGTCCCTTTT CTTTCGCCGC TTCAACTTTT TTTTTTTTAT CTTACACACA TCACGACCAT    1200
GACTGTACAC GATATTATCG CCACATACTT CACCAAATGG TACGTGATAG TACCACTCGC    1260
TTTGATTGCT TATAGAGTCC TCGACTACTT CTATGGCAGA TACTTGATGT ACAAGCTTGG    1320
TGCTAAACCA TTTTTCCAGA AACAGACAGA CGGCTGTTTC GGATTCAAAG CTCCGCTTGA    1380
ATTGTTGAAG AAGAAGAGCG ACGGTACCCT CATAGACTTC ACACTCCAGC GTATCCACGA    1440
TCTCGATCGT CCCGATATCC CAACTTTCAC ATTCCCGGTC TTTTCCATCA ACCTTGTCAA    1500
TACCCTTGAG CCGGAGAACA TCAAGGCCAT CTTGGCCACT CAGTTCAACG ATTTCTCCTT    1560
GGGTACCAGA CACTCGCACT TTGCTCCTTT GTTGGGTGAT GGTATCTTTA CGTTGGATGG    1620
CGCCGGCTGG AAGCACAGCA GATCTATGTT GAGACCACAG TTTGCCAGAG AACAGATTTC    1680
CCACGTCAAG TTGTTGGAGC CACACGTTCA GGTGTTCTTC AAACACGTCA GAAAGGCACA    1740
GGGCAAGACT TTTGACATCC AGGAATTGTT TTTCAGATTG ACCGTCGACT CCGCCACCGA    1800
GTTTTTGTTT GGTGAATCCG TTGAGTCCTT GAGAGATGAA TCTATCGGCA TGTCCATCAA    1860
TGCGCTTGAC TTTGACGGCA AGGCTGGCTT TGCTGATGCT TTTAACTATT CGCAGAATTA    1920
TTTGGCTTCG AGAGCGGTTA TGCAACAATT GTACTGGGTG TTGAACGGGA AAAAGTTTAA    1980
GGAGTGCAAC GCTAAAGTGC ACAAGTTTGC TGACTACTAC GTCAACAAGG CTTTGGACTT    2040
GACGCCTGAA CAATTGGAAA AGCAGGATGG TTATGTGTTT TTGTACGAAT TGGTCAAGCA    2100
AACCAGAGAC AAGCAAGTGT TGAGAGACCA ATTGTTGAAC ATCATGGTTG CTGGTAGAGA    2160
CACCACCGCC GGTTTGTTGT CGTTTGTTTT CTTTGAATTG GCCAGAAACC CAGAAGTTAC    2220
CAACAAGTTG AGAGAAGAAA TTGAGGACAA GTTTGGACTC GGTGAGAATG CTAGTGTTGA    2280
AGACATTTCC TTTGAGTCGT TGAAGTCCTG TGAATACTTG AAGGCTGTTC TCAACGAAAC    2340
CTTGAGATTG TACCCATCCG TGCCACAGAA TTTCAGAGTT GCCACCAAGA ACACTACCCT    2400
CCCAAGAGGT GGTGGTAAGG ACGGGTTGTC TCCTGTTTTG GTGAGAAAGG GTCAGACCGT    2460
TATTTACGGT GTCTACGCAG CCCACAGAAA CCCAGCTGTT TACGGTAAGG ACGCTCTTGA    2520
GTTTAGACCA GAGAGATGGT TTGAGCCAGA GACAAAGAAG CTTGGCTGGG CCTTCCTCCC    2580
ATTCAACGGT GGTCCAAGAA TCTGTTTGGG ACAGCAGTTT GCCTTGACAG AAGCTTCGTA    2640
TGTCACTGTC AGGTTGCTCC AGGAGTTTGC ACACTTGTCT ATGGACCCAG ACACCGAATA    2700
TCCACCTAAG AAAATGTCGC ATTTGACCAT GTCGCTTTTC GACGGTGCCA ATATTGAGAT    2760
GTATTAGAGG GTCATGTGTT ATTTTGATTG TTTAGTTTGT AATTACTGAT TAGGTTAATT    2820
CATGGATTGT TATTTATTGA TAGGGGTTTG CGCGTGTTGC ATTCACTTGG GATCGTTCCA    2880
GGTTGATGTT TCCTTCCATC CTGTCGAGTC AAAAGGAGTT TTGTTTTGTA ACTCCGGACG    2940
ATGTTTTAAA TAGAAGGTCG ATCTCCATGT GATTGTTTTG ACTGTTACTG TGATTATGTA    3000
ATCTGCGGAC GTTATACAAG CATGTGATTG TGGTTTTGCA GCCTTTTGCA CGACAAATGA    3060
TCGTCAGACG ATTACGTAAT CTTTGTTAGA GGGGTAAAAA AAAACAAAAT GGCAGCCAGA    3120
ATTTCAAACA TTCTGCAAAC AATGCAAAAA ATGGGAAACT CCAACAGACA AAAAAAAAAA    3180
CTCCGCAGCA CTCCGAACCC ACAGAACAAT GGGGCGCCAG AATTATTGAC TATTGTGACT    3240
TTTTTACGCT AACGCTCATT GCAGTGTAGT GCGTCTTACA CGGGGTATTG CTTTCTACAA    3300
TGCAAGGGCA CAGTTGAAGG TTTGCACCTA ACGTTGCCCC GTGTCAACTC AATTTGACGA    3360
GTAACTTCCT AAGCTCGAAT TATGCAGCTC GTGCGTCAAC CTATGTGCAG GAAAGAAAAA    3420
ATCCAAAAAA ATCGAAAATG CGACTTTCGA TTTTGAATAA ACCAAAAAGA AAAATGTCGC    3480
ACTTTTTTCT CGCTCTCGCT CTCTCGACCC AAATCACAAC AAATCCTCGC GCGCAGTATT    3540
TCGACGAAAC CACAACAAAT AAAAAAAACA AATTCTACAC CACTTCTTTT TCTTCACCAG    3600
TCAACAAAAA ACAACAAATT ATACACCATT TCAACGATTT TTGCTCTTAT AAATGCTATA    3660
TAATGGTTTA ATTCAACTCA GGTATGTTTA TTTTACTGTT TTCAGCTCAA GTATGTTCAA    3720
ATACTAACTA CTTTTGATGT TTGTCGCTTT TCTAGAATCA AAACAACGCC CACAACACGC    3780
CGAGCTTGTC GAATAGACGG TTTGTTTACT CATTAGATGG TCCCAGATTA CTTTTCAAGC    3840
CAAAGTCTCT CGAGTTTTGT TTGCTGTTTC CCCAATTCCT AACTATGAAG GGTTTTTATA    3900
AGGTCCAAAG ACCCCAAGGC ATAGTTTTTT TGGTTCCTTC TTGTCGTG                 3948
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(2) INFORMATION FOR SEQ ID NO:87:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 3755 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

GCTCAACAAT TGTCTGACAA GATCTCGCAA CACAAGGCTA ACGCCTGGTT GTTGAACACT 60
GGTTGGGTTG GTTCTTCTGC TGCTAGAGGT GGTAAGAGAT GTTCATTGAA GTACACCAGA 120
GCCATTTTGG ACGCTATCCA CTCTGGTGAA TTGTCCAAGG TTGAATACGA GACTTTCCCA 180
GTCTTCAACT TGAATGTCCC AACCTCCTGC CCAGGTGTCC CAAGTGAAAT CTTGAACCCA 240
ACCAAGGCCT GGACCGAAGG TGTTGACTCC TTCAACAAGG AAATCAAGTC TTTGGCTGGT 300
AAGTTTGCTG AAAACTTCAA GACCTATGCT GACCAAGCTA CCGCTGAAGT TAGAGCTGCA 360
GGTCCAGAAG CTTAAAGATA TTTATTCACT ATTTAGTTTG CCTATTTATT TCTCATCACC 420
CATCATCATT CAACAATATA TATAAAGTTA TTTCGGAACT CATATATCAT TGTAATCGTG 480
CGTGTTGCAA TTGGGTAATT TGAAACTGTA GTTGGAACGG ATTCATGCAC GATGCGGAGA 540
TAACACGAGA TTATCTCCTA AGACAATTTT GGCCTCATTC ACACGCCCTT CTTCTGAGCT 600
AAGGATAAAT AATTAGACTT CACAAGTTCA TTAAAATATC CGTCACGCGA AAACTGCAAC 660
AATAAGGAAG GGGGGGGTAG ACGTAGCCGA TGAATGTGGG GTGCCAGTAA ACGCAGTCTC 720
TCTCTCCCCC CCCCCCCCCC CCCCCTCAGG AATAGTACAA CGGGGGAAGG ATAACGGATA 780
GCAAGTGGAA TGCGAGGAAA ATTTTGAATG CGCAAGGAAA GCAATATCCG GGCTATCAGG 840
TTTTGAGCCA GGGGACACAC TCCTCTTCTG CACAAAAACT TAACGTAGAC AAAAAAAAAA 900
AACTCCACCA AGACACAATG AATCGCACAT GGACATTTAG ACCTCCCCAC ATGTGAAAGC 960
TTCTCTGGCG AAAGCAAAAA AAGTATAATA AGGACCCATG CCTTCCCTCT TCCTGGGCCG 1020
TTTCAACTTT TTCTTTTTCT TTGTCTATCA ACACACACAC ACCTCACGAC CATGACTGCA 1080
CAGGATATTA TCGCCACATA CATCACCAAA TGGTACGTGA TAGTACCACT CGCTTTGATT 1140
GCTTATAGGG TCCTCGACTA CTTTTACGGC AGATACTTGA TGTACAAGCT TGGTGCTAAA 1200
CCGTTTTTCC AGAAACAAAC AGACGGTTAT TTCGGATTCA AAGCTCCACT TGAATTGTTA 1260
AAAAAGAAGA GTGACGGTAC CCTCATAGAC TTCACTCTCG AGCGTATCCA AGCGCTCAAT 1320
CGTCCAGATA TCCCAACTTT TACATTCCCA ATCTTTTCCA TCAACCTTAT CAGCACCCTT 1380
GAGCCGGAGA ACATCAAGGC TATCTTGGCC ACCCAGTTCA ACGATTTCTC CTTGGGCACC 1440
AGACACTCGC ACTTTGCTCC TTTGTTGGGC GATGGTATCT TTACCTTGGA CGGTGCCGGC 1500
TGGAAGCACA GCAGATCTAT GTTGAGACCA CAGTTTGCCA GAGAACAGAT TTCCCACGTC 1560
AAGTTGTTGG AGCCACACAT GCAGGTGTTC TTCAAGCACG TCAGAAAGGC ACAGGGCAAG 1620
ACTTTTGACA TCCAAGAATT GTTTTTCAGA TTGACCGTCG ACTCCGCCAC TGAGTTTTTG 1680
TTTGGTGAAT CCGTTGAGTC CTTGAGAGAT GAATCTATTG GGATGTCCAT CAATGCACTT 1740
GACTTTGACG GCAAGGCTGG CTTTGCTGAT GCTTTTAACT ACTCGCAGAA CTATTTGGCT 1800
TCGAGAGCGG TTATGCAACA ATTGTACTGG GTGTTGAACG GGAAAAAGTT TAAGGAGTGC 1860
AACGCTAAAG TGCACAAGTT TGCTGACTAT TACGTCAGCA AGGCTTTGGA CTTGACACCT 1920
GAACAATTGG AAAAGCAGGA TGGTTATGTG TTCTTGTACG AGTTGGTCAA GCAAACCAGA 1980
GACAGGCAAG TGTTGAGAGA CCAGTTGTTG AACATCATGG TTGCCGGTAG AGACACCACC 2040
GCCGGTTTGT TGTCGTTTGT TTTCTTTGAA TTGGCCAGAA ACCCAGAGGT GACCAACAAG 2100
TTGAGAGAAG AAATCGAGGA CAAGTTTGGT CTTGGTGAGA ATGCTCGTGT TGAAGACATT 2160
TCCTTTGAGT CGTTGAAGTC ATGTGAATAC TTGAAGGCTG TTCTCAACGA AACTTTGAGA 2220
TTGTACCCAT CCGTGCCACA GAATTTCAGA GTTGCCACCA AAAACACTAC CCTTCCAAGG 2280
GGAGGTGGTA AGGACGGGTT ATCTCCTGTT TTGGTCAGAA AGGGTCAAAC CGTTATGTAC 2340
GGTGTCTACG CTGCCCACAG AAACCCAGCT GTCTACGGTA AGGACGCCCT TGAGTTTAGA 2400
CCAGAGAGGT GGTTTGAGCC AGAGACAAAG AAGCTTGGCT GGGCCTTCCT TCCATTCAAC 2460
GGTGGTCCAA GAATTTGCTT GGGACAGCAG TTTGCCTTGA CAGAAGCTTC GTATGTCACT 2520
GTCAGATTGC TCCAAGAGTT TGGACACTTG TCTATGGACC CCAACACCGA ATATCCACCT 2580
AGGAAAATGT CGCATTTGAC CATGTCCCTT TTCGACGGTG CCAACATTGA GATGTATTAG 2640
AGGATCATGT GTTATTTTTG ATTGGTTTAG TCTGTTTGTA GCTATTGATT AGGTTAATTC 2700
ACGGATTGTT ATTTATTGAT AGGGGGTGCG TGTGTGTGTG TGTGTTGCAT TCACATGGGA 2760
TCGTTCCAGG TTGTTGTTTC CTTCCATCCT GTTGAGTCAA AAGGAGTTTT GTTTTGTAAC 2820
TCCGGACGAT GTCTTAGATA GAAGGTCGAT CTCCATGTGA TTGTTTGACT GCTACTCTGA 2880
TTATGTAATC TGTAAAGCCT AGACGTTATG CAAGCATGTG ATTGTGGTTT TTGCAACCTG 2940
TTTGCACGAC AAATGATCGA CAGTCGATTA CGTAATCCAT ATTATTTAGA GGGGTAATAA 3000
AAAATAAATG GCAGCCAGAA TTTCAAACAT TTTGCAAACA ATGCAAAAGA TGAGAAACTC 3060
CAACAGAAAA AATAAAAAAA CTCCGCAGCA CTCCGAACCA ACAAAACAAT GGGGGGCGCC 3120
AGAATTATTG ACTATTGTGA CTTTTTTTTA TTTTTTCCGT TAACTTTCAT TGCAGTGAAG 3180
TGTGTTACAC GGGGTGGTGA TGGTGTTGGT TTCTACAATG CAAGGGCACA GTTGAAGGTT 3240
TCCACATAAC GTTGCACCAT ATCAACTCAA TTTATCCTCA TTCATGTGAT AAAAGAAGAG 3300

CCAAAAGGTA ATTGGCAGAC CCCCCAAGGG GAACACGGAG TAGAAAGCAA TGGAAACACG 3360
CCCATGACAG TGCCATTTAG CCCACAACAC ATCTAGTATT CTTTTTTTTT TTTGTGCGCA 3420
GGTGCACACC TGGACTTTAG TTATTGCCCC ATAAAGTTAA CAATCTCACC TTTGGCTCTC 3480
CCAGTGTCTC CGCCTCCAGA TGCTCGTTTT ACACCCTCGA GCTAACGACA ACACAACACC 3540
CATGAGGGGA ATGGGCAAAG TTAAACACTT TTGGTTTCAA TGATTCCTAT TTGCTACTCT 3600
CTTGTTTTGT GTTTTGATTT GCACCATGTG AAATAAACGA CAATTATATA TACCTTTTCG 3660
TCTGTCCTCC AATGTCTCTT TTTGCTGCCA TTTTGCTTTT TGCTTTTTGC TTTTGCACTC 3720
TCTCCCACTC CCACAATCAG TGCAGCAACA CACAA 3755

(2) INFORMATION FOR SEQ ID NO:88:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3900 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA (genomic)
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

GACATCATAA TGACCCGGTT ATTTCGCCCT CAGGTTGCTT ATTTGAGCCG TAAAGTGCAG 60
TAGAAACTTT GCCTTGGGTT CAAACTCTAG TATAATGGTG ATAACTGGTT GCACTCTTGC 120
CATAGGCATG AAAATAGGCC GTTATAGTAC TATATTTAAT AAGCGTAGGA GTATAGGATG 180
CATATGACCG GTTTTTCTAT ATTTTTAAGA TAATCTCTAG TAAATTTTGT ATTCTCAGTA 240
GGATTTCATC AAATTTCGCA ACCAATTCTG GCGAAAAAAT GATTCTTTTA CGTCAAAAGC 300
TGAATAGTGC AGTTTAAAGC ACCTAAAATC ACATATACAG CCTCTAGATA CGACAGAGAA 360
GCTCTTTATG ATCTGAAGAA GCATTAGAAT AGCTACTATG AGCCACTATT GGTGTATATA 420
TTAGGGATTG GTGCAATTAA GTACGTACTA ATAAACAGAA GAAAATACTT AACCAATTTC 480
TGGTGTATAC TTAGTGGTGA GGGACCTTTT CTGAACATTC GGGTCAAACT TTTTTTTGGA 540
GTGCGACATC GATTTTTCGT TTGTGTAATA ATAGTGAACC TTTGTGTAAT AAATCTTCAT 600
GCAAGACTTG CATAATTCGA GCTTGGGAGT TCACGCCAAT TTGACCTCGT TCATGTGATA 660
AAAGAAAAGC CAAAAGGTAA TTAGCAGACG CAATGGGAAC ATGGAGTGGA AAGCAATGGA 720
AGCACGCCCA GGACGGAGTA ATTTAGTCCA CACTACATCT GGGGGTTTTT TTTTTGTGCG 780
CAAGTACACA CCTGGACTTT AGTTTTTGCC CCATAAAGTT AACAATCTAA CCTTTGGCTC 840
TCCAACTCTC TCCGCCCCCA AATATTCGTT TTTACACCCT CAAGCTAGCG ACAGCACAAC 900
ACCCATTAGA GGAATGGGGC AAAGTTAAAC ACTTTTGGCT TCAATGATTC CTATTCGCTA 960
CTACATTCTT CTCTTGTTTT GTGCTTTGAA TTGCACCATG TGAAATAAAC GACAATTATA 1020
TATACCTTTT CATCCCTCCT CCTATATCTC TTTTTGCTAC ATTTTGTTTT TTACGTTTCT 1080
TGCTTTTGCA CTCTCCCACT CCCACAAAGA AAAAAAAACT ACACTATGTC GTCTTCTCCA 1140
TCGTTTGCCC AAGAGGTTCT CGCTACCACT AGTCCTTACA TCGAGTACTT TCTTGACAAC 1200
TACACCAGAT GGTACTACTT CATACCTTTG GTGCTTCTTT CGTTGAACTT TATAAGTTTG 1260
CTCCACACAA GGTACTTGGA ACGCAGGTTC CACGCCAAGC CACTCGGTAA CTTTGTCAGG 1320
GACCCTACGT TTGGTATCGC TACTCCGTTG CTTTTGATCT ACTTGAAGTC GAAAGGTACG 1380
GTCATGAAGT TTGCTTGGGG CCTCTGGAAC AACAAGTACA TCGTCAGAGA CCCAAAGTAC 1440
AAGACAACTG GGCTCAGGAT TGTTGGCCTC CCATTGATTG AAACCATGGA CCCAGAGAAC 1500
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AGAACTATGT TGAGACCACA GTTTGCTAGA GAACAGGTTT CTCACGTCAA GTTGTTGGAG 1680
CCACACGTTC AGGTGTTCTT CAAGCACGTT AGAAAGCACC GCGGTCAAAC GTTCGACATC 1740
CAAGAATTGT TCTTCAGGTT GACCGTCGAC TCCGCCACCG AGTTCTTGTT TGGTGAGTCT 1800
GCTGAATCCT TGAGGGACGA ATCTATTGGA TTGACCCCAA CCACCAAGGA TTTCGATGGC 1860
AGAAGAGATT TCGCTGACGC TTTCAACTAT TCGCAGACTT ACCAGGCCTA CAGATTTTTG 1920
TTGCAACAAA TGTACTGGAT CTTGAATGGC TCGGAATTCA GAAAGTCGAT TGCTGTCGTG 1980
CACAAGTTTG CTGACCACTA TGTGCAAAAG GCTTTGGAGT TGACCGACGA TGACTTGCAG 2040
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TTGAGAGACC AGTTATTGAA CATTTTGGTT GCCGGTAGAG ACACGACCGC CGGTTTGTTG 2160
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GTGGAAAACA GATTTGGACT CGGTGAAGAA GCTCGTGTTG AAGAGATCTC GTTTGAGTCC 2280
TTGAAGTCTT GTGAGTACTT GAAGGCTGTC ATCAATGAAA CCTTGAGATT GTACCCATCG 2340

GTTCCACACA ACTTTAGAGT TGCTACCAGA AACACTACCC TCCCAAGAGG TGGTGGTGAA 2400
GATGGATACT CGCCAATTGT CGTCAAGAAG GGTCAAGTTG TCATGTACAC TGTTATTGCT 2460
ACCCACAGAG ACCCAAGTAT CTACGGTGCC GACGCTGACG TCTTCAGACC AGAAAGATGG 2520
TTTGAACCAG AAACTAGAAA GTTGGGCTGG GCATACGTTC CATTCAATGG TGGTCCAAGA 2580
ATCTGTTTGG GTCAACAGTT TGCCTTGACC GAAGCTTCAT ACGTCACTGT CAGATTGCTC 2640
CAGGAGTTTG CACACTTGTC TATGGACCCA GACACCGAAT ATCCACCAAA ATTGCAGAAC 2700
ACCTTGACCT TGTCGCTCTT TGATGGTGCT GATGTTAGAA TGTACTAAGG TTGCTTTTCC 2760
TTGCTAATTT TCTTCTGTAT AGCTTGTGTA TTTAAATTGA ATCGGCAATT GATTTTTCTG 2820
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CGTGCTCGCT CATCAGCACT GTTTGAAGAC GAAAGAGAAA ATTTTTTGTA AACAACACTG 2940
TCCAAATTTA CCCAACGTGA ACCATTATGC AAATGAGCGG CCCTTTCAAC TGGTCGCTGG 3000
AAGCATTCGG GGATATCTAC AACGCCCTTA AGTTTGAAAC AGACATTGAT TTAGACACCA 3060
TAGATTTCAG CGGCATCAAG AATGACCTTG CCCACATTTT GACGACCCCA ACACCACTGG 3120
AAGAATCACG CCAGAAACTA GGCGATGGAT CCAAGCCTGT GACCTTGCCC AATGGAGACG 3180
AAGTGGAGTT GAACCAAGCG TTCCTAGAAG TTACCACATT ATTGTCGAAT GAGTTTGACT 3240
TGGACCAATT GAACGCGGCA GAGTTGTTAT ACTACGCTGG CGACATATCC TACAAGAAGG 3300
GCACATCAAT CGCAGACAGT GCCAGATTGT CTTATTATTT GAGAGCAAAC TACATCTTGA 3360
ACATACTTGG GTATTTGATT TCGAAGCAGC GATTGGATTT GATAGTCACG GACAACGACG 3420
CGTTGTTTGA TAGTATTTTG AAAAGTTTTG AAAAGATCTA CAAGTTGATA AGCGTGTTGA 3480
ACGATATGAT TGACAAGCAA AAGGTGACAA GCGACATCAA CAGTCTAGCA TTCATCAATT 3540
GCATCAACTA CTCGAGAGGT CAACTATTCT CCGCACACGA ACTTTTGGGA CTGGTTTTGT 3600
TTGGATTGGT CGACATCTAT TTCAACCAGT TTGGCACATT AGACAACTAC AAGAAGGTAT 3660
TGGCATTGAT ACTGAAGAAC ATCAGCGATG AAGACATCTT GATCATACAC TTCCTCCCAT 3720
CGACACTACA ATTGTTTAAG CTGGTGTTGG ACAAGAAAGA CGACGCTGCA GTTGAACAGT 3780
TCTACAAGTA CATCACTTCA ACAGTGTCAC GAGACTACAA CTCCAACATC GGCTCCACAG 3840
CCAAAGATGA TATCGATTTG TCCAAAACCA AACTCAGTGG CTTTGAGGTG TTGACGAGTT 3900

(2) INFORMATION FOR SEQ ID NO:89:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3668 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA (genomic)
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

CCTGCAGAAT TCGCGGCCGC GTCGACAGAG TAGCAGTTAT GCAAGCATGT GATTGTGGTT 60
TTTGCAACCT GTTTGCACGA CAAATGATCG ACAGTCGATT ACGTAATCCA TATTATTTAG 120
AGGGGTAATA AAAAATAAAT GGCAGCCAGA ATTTCAAACA TTTTGCAAAC AATGCAAAAG 180
ATGAGAAACT CCAACAGAAA AAATAAAAAA ACTCCGCAGC ACTCCGAACC AACAAAACAA 240
TGGGGGGCGC CAGAATTATT GACTATTGTG ACTTTTTTTT ATTTTTTCCG TTAACTTTCA 300
TTGCAGTGAA GTGTGTTACA CGGGGTGGTG ATGGTGTTGG TTTCTACAAT GCAAGGGCAC 360
AGTTGAAGGT TTCCACATAA CGTTGCACCA TATCAACTCA ATTTATCCTC ATTCATGTGA 420
TAAAAGAAGA GCCAAAAGGT AATTGGCAGA CCCCCCAAGG GGAACACGGA GTAGAAAGCA 480
ATGGAAACAC GCCCATGACA GTGCCATTTA GCCCACAACA CATCTAGTAT TCTTTTTTTT 540
TTTTGTGCGC AGGTGCACAC CTGGACTTTA GTTATTGCCC CATAAAGTTA ACAATCTCAC 600
CTTTGGCTCT CCCAGTGTCT CCGCCTCCAG ATGCTCGTTT TACACCCTCG AGCTAACGAC 660
AACACAACAC CCATGAGGGG AATGGGCAAA GTTAAACACT TTTGGTTTCA ATGATTCCTA 720
TTTGCTACTC TCTTGTTTTG TGTTTTGATT TGCACCATGT GAAATAAACG ACAATTATAT 780
ATACCTTTTC GTCTGTCCTC CAATGTCTCT TTTTGCTGCC ATTTTGCTTT TTGCTTTTTG 840
CTTTTGCACT CTCTCCCACT CCCACAATCA GTGCAGCAAC ACACAAAGAA GAAAAATAAA 900
AAAACCTACA CTATGTCGTC TTCTCCATCG TTTGCTCAGG AGGTTCTCGC TACCACTAGT 960
CCTTACATCG AGTACTTTCT TGACAACTAC ACCAGATGGT ACTACTTCAT CCCTTTGGTG 1020
CTTCTTTCGT TGAACTTCAT CAGCTTGCTC CACACAAAGT ACTTGGAACG CAGGTTCCAC 1080
GCCAAGCCGC TCGGTAACGT CGTGTTGGAT CCTACGTTTG GTATCGCTAC TCCGTTGATC 1140
TTGATCTACT TAAAGTCGAA AGGTACAGTC ATGAAGTTTG CCTGGAGCTT CTGGAACAAC 1200
AAGTACATTG TCAAAGACCC AAAGTACAAG ACCACTGGCC TTAGAATTGT CGGCCTCCCA 1260

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TTGATTGAAA CCATAGACCC AGAGAACATC AAAGCTGTGT TGGCTACTCA GTTCAACGAT    1320
TTCTCCTTGG GAACTAGACA CGATTTCTTG TACTCCTTGT TGGGCGATGG TATTTTTACC    1380
TTGGACGGTG CTGGCTGGAA ACACAGTAGA ACTATGTTGA GACCACAGTT TGCTAGAGAA    1440
CAGGTTTCCC ACGTCAAGTT GTTGGAACCA CACGTTCAGG TGTTCTTCAA GCACGTTAGA    1500
AAACACCGCG GTCAGACTTT TGACATCCAA GAATTGTTCT TCAGATTGAC CGTCGACTCC    1560
GCCACCGAGT TCTTGTTTGG TGAGTCTGCT GAATCCTTGA GAGACGACTC TGTTGGTTTG    1620
ACCCCAACCA CCAAGGATTT CGAAGGCAGA GGAGATTTCG CTGACGCTTT CAACTACTCG    1680
CAGACTTACC AGGCCTACAG ATTTTTGTTG CAACAAATGT ACTGGATTTT GAATGGCGCG    1740
GAATTCAGAA AGTCGATTGC CATCGTGCAC AAGTTTGCTG ACCACTATGT GCAAAAGGCT    1800
TTGGAGTTGA CCGACGATGA CTTGCAGAAA CAAGACGGCT ATGTGTTCTT GTACGAGTTG    1860
GCTAAGCAAA CTAGAGACCC AAAGGTCTTG AGAGACCAGT TGTTGAACAT TTTGGTTGCC    1920
GGTAGAGACA CGACCGCCGG TTTGTTGTCG TTTGTGTTCT ACGAGTTGTC GAGAAACCCT    1980
GAAGTGTTTG CCAAGTTGAG AGAGGAGGTG GAAAACAGAT TTGGACTCGG CGAAGAGGCT    2040
CGTGTTGAAG AGATCTCTTT TGAGTCCTTG AAGTCCTGTG AGTACTTGAA GGCTGTCATC    2100
AATGAAGCCT TGAGATTGTA CCCATCTGTT CCACACAACT TCAGAGTTGC CACCAGAAAC    2160
ACTACCCTTC CAAGAGGCGG TGGTAAAGAC GGATGCTCGC CAATTGTTGT CAAGAAGGGT    2220
CAAGTTGTCA TGTACACTGT CATTGGTACC CACAGAGACC CAAGTATCTA CGGTGCCGAC    2280
GCCGACGTCT TCAGACCAGA AAGATGGTTC GAGCCAGAAA CTAGAAAGTT GGGCTGGGCA    2340
TATGTTCCAT TCAATGGTGG TCCAAGAATC TGTTTGGGTC AGCAGTTTGC CTTGACTGAA    2400
GCTTCATACG TCACTGTCAG ATTGCTCCAA GAGTTTGGAA ACTTGTCCCT GGATCCAAAC    2460
GCTGAGTACC CACCAAAATT GCAGAACACC TTGACCTTGT CACTCTTTGA TGGTGCTGAC    2520
GTTAGAATGT TCTAAGGTTG CTTATCCTTG CTAGTGTTAT TTATAGTTTG TGTATTTAAA    2580
TTGAATCGGC GATTGATTTT TCTGGTACTA ATAACTGTAG TGGGTTTTGA CCAAAACCGT    2640
TCAAACTTTT TTTTTTTTTT TCTTCCCCCT ACCTTCGTTG CTCGCTCATC AGCACTGTTT    2700
GAAAACGAAA AAAGAAAATT TTTTGTAAAC AACATTGCCC AAACTTACCC AACGTGAACC    2760
ATTATAACCA AATGAGCGGC GCTTTCAACT GGTCACTGGA GGCATTCGGG GATATCTACA    2820
ACACCCTTAA GTTTGAGGAA GACATTGATT TAGACACCAT AGATTTCAGC GGCATCAAGA    2880
ATGACCTTGT CCACATTTTG ACAACCCCAA CACCACTGGA AGAATCGCGC CAGAAACTAG    2940
GCGATGGATC CAAGCCTGTG GCCTTGCCCA ATGGAGACGA AGTGGAGTTG AACCAAGCGT    3000
TCCTAGAAGT TACCACATTA TTGTCGAACG AGTTTGACTT GGACCAATTG AACGCGGCCG    3060
AGTTGTTATA CTACGCCGGC GACATATCCT ACAAGAAGGG CACATCAATT GCCGACAGTG    3120
CCAGATTGTC TTACTATTTG AGAGCAAACT ACATCTTGAA CATACTTGGG TACTTTATTT    3180
CGAAGCAGCG ATTGGATGTG ATAGTCACCG ACAACAACGC GTTGTTTGAT AATATTTTGA    3240
AAAGTTTTGA AAAGATCTAC AAGTTGATAA GCGCGTTGAA CGATATGATT GACAAGCAAA    3300
AGGTGACAAG CGACATCAAC AGTCTAGCAT TTATCAACTG CATCAACTAC TCGAGGGGTC    3360
AACTATTCTC CGCACACGAA CTTTTGGGAC TGGTTTTGTT TGGATTGGTT GACAACTATT    3420
TCAACCAGTT TGGCTCATTA GACAACTACA AGAAAGTATT GGCATTGATA CTGAAGAACA    3480
TCAGTGATGA AGATATCTTG ATCGTACGCT TCCTCCCATC GACACTACAA TTGTTTAAGC    3540
TGGTGTTGGA TAAGAAAGAC GACGCCACTG TTGACCAGTT CTACAAGTAC ATCACCTCAA    3600
CAGTGTCGCA AGACTACAAC TCCAACATCG GAGCCACAGC CAAAGATGAT ATCGATTTGT    3660
CCAAAGCC                                                            3668
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(2) INFORMATION FOR SEQ ID NO:90:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 3826 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

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GCAACACGAC GTTGCCACGC GGAGGAGGCA AAGACGGCAA GGAACCTATC TTGGTGCAGA     180
AGGGACAGTC CGTTGGGTTG ATTACTATTG CCACGCAGAC GGACCCAGAG TATTTTGGGG     240
CCGACGCTGG TGAGTTTAAG CCGGAGAGAT GGTTTGATTC AAGCATGAAG AACTTGGGGT     300
GTAAATACTT GCCGTTCAAT GCTGGGCCAC GGACTTGCTT GGGGCAGCAG TACACTTTGA     360
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TTGAAGCGAG CTACTTGCTA GTCCGGTTGG CCCAGACCTA CCGGGCAATA GATTTGCAGC     420
CAGGATCGGC GTACCCACCA AGAAAGAAGT CGTTGATCAA CATGAGTGCT GCCGACGGGG     480
TGTTTGTAAA GCTTTATAAG GATGTAACGG TAGATGGATA GTTGTGTAGG AGGAGCGGAG     540
ATAAATTAGA TTTGATTTTG TGTAAGGTTT TGGATGTCAA CCTACTCCGC ACTTCATGCA     600
GTGTGTGTGA CACAAGGGTG TACTACGTGT GCGTGTGCGC CAAGAGACAG CCCAAGGGGG     660
TGGTAGTGTG TGTTGGCGGA AGTGCATGTG ACACAACGCG TGGGTTCTGG CCAATGGTGG     720
ACTAAGTGCA GGTAAGCAGC GACCTGAAAC ATTCCTCAAC GCTTAAGACA CTGGTGGTAG     780
AGATGCGGAC CAGGCTATTC TTGTCGTGCT ACCCGGCGCA TGGAAAATCA ACTGCGGGAA     840
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ACGCCGCCAC TAACTACATC ACTCCCCTAT TTTCTCTCTC TCTCTTTGTC TTACTCCGCT     960
CCCGTTTCCT TAGCCACAGA TACACACCCA CTGCAAACAG CAGCAACAAT TATAAAGATA    1020
CGCCAGGCCC ACCTTCTTTC TTTTTCTTCA CTTTTTTGAC TGCAACTTTC TACAATCCAC    1080
CACAGCCACC ACCACAGCCG CTATGATTGA ACAACTCCTA GAATATTGGT ATGTCGTTGT    1140
GCCAGTGTTG TACATCATCA AACAACTCCT TGCATACACA AAGACTCGCG TCTTGATGAA    1200
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TGGATGGAAG GCTCTCCAGT TCAAGAAAGA GGGCAGGGCT CAAGAGTACA ACGATTACAA    1320
GTTTGACCAC TCCAAGAACC CAAGCGTGGG CACCTACGTC AGTATTCTTT TCGGCACCAG    1380
GATCGTCGTG ACCAAAGATC CAGAGAATAT CAAAGCTATT TTGGCAACCC AGTTTGGTGA    1440
TTTTTCTTTG GGCAAGAGGC ACACTCTTTT TAAGCCTTTG TTAGGTGATG GGATCTTCAC    1500
ATTGGACGGC GAAGGCTGGA AGCACAGCAG AGCCATGTTG AGACCACAGT TTGCCAGAGA    1560
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CAACCAAGAC GATATAGATT TTGCTGGTAG AAAGGACTTT GCTGAGTCGT TCAACAAAGC    1800
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TTTGGATGCT AGCCCAGAAG AGCTTGAAAA GCAAAGTGGG TATGTGTTCT TGTACGAGCT    1980
TGTCAAGCAG ACAAGAGACC CCAATGTGTT GCGTGACCAG TCTTTGAACA TCTTGTTGGC    2040
CGGAAGAGAC ACCACTGCTG GGTTGTTGTC GTTTGCTGTC TTTGAGTTGG CCAGACACCC    2100
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TCGTGTTGAA GAGATTACCT TTGAGAGCTT GAAGAGATGT GAGTACTTGA AAGCGTTCCT    2220
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GAAGAAACTC GCAGAATTGA CCATCCAGAA CCAGCCATCC AGCTTGAAAG AAATCAACAC    3300
CGGCATCCAG AAGGACGACT TTGCCAAGTT GTTGTCTGCC ACCCCGAAAA TCCCCACCAA    3360
GCACAAGTTG AACGGCAACC ACGAATTGTC TGAGGTCGCC ATTGCCAAAA AGGAGTACGA    3420
GGTGTTGATT GCCTTGAGCG ACGCCACAAA AGACCCAATC AAAGTGACCT CCCAGATCAA    3480
GATCTTGATT GACAAGTTCA AGGTGTACTT GTTTGAGTTG CCTGACCAGA AGTTCTCCTA    3540
CTCCATCGTG TCCAACTCCG TCAACATCGC CCCCTGGACC TTGCTCGGGG AGAAGTTGAC    3600
CACGGGCTTG ATCAACTTGG CCTTCCAGAA CAACAAGCAG CACTTGGACG AGGTCATTGA    3660
CATCTTCAAC GAGTTCATCG ACAAGTTCTT TGGCAACACG GAGCCGCAAT TGACCAACTT    3720
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CTTGACCTTG TGCGGTGTGT TGGACGGGTT GATTGACCAT GCCAACTTCT TGAGCGTGTC 3780
CTCGCGGACC TTCAAGATCT TCTTGAACTT GGACTCGTAT GTGGAC 3826

(2) INFORMATION FOR SEQ ID NO:91:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3910 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA (genomic)
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

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AGTACGTTCA GGCGGTGCTC AACGAAACGC TTCGTATCTA CCCGGGGGTG CCACGAAACA 180
TGAAGACAGC TACGTGCAAC ACGACGTTGC CGCGTGGAGG AGGCAAAGAC GGTAAGGAAC 240
CTATTTTGGT GCAGAAGGGC CAGTCCGTTG GGTTGATTAC TATTGCCACG CAGACGGACC 300
CAGAGTATTT TGGGGCAGAT GCTGGTGAGT TCAAACCGGA GAGATGGTTT GATTCAAGCA 360
TGAAGAACTT GGGGTGTAAG TACTTGCCGT TCAATGCTGG GCCCCGGACT TGTTTGGGGC 420
AGCAGTACAC TTTGATTGAA GCGAGCTATT TGCTAGTCAG GTTGGCGCAG ACCTACCGGG 480
TAATCGATTT GCTGCCAGGG TCGGCGTACC CACCAAGAAA GAAGTCGTTG ATCAATATGA 540
GTGCTGCCGA TGGGGTGGTT GTAAAGTTTC ACAAGGATCT AGATGGATAT GTAAGGTGTG 600
TAGGAGGAGC GGAGATAAAT TAGATTTGAT TTTGTGTAAG GTTTAGCACG TCAAGCTACT 660
CCGCACTTTG TGTGTAGGGA GCACATACTC CGTCTGCGCC TGTGCCAAGA GACGGCCCAG 720
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GAGATGCGGG CCAGGAGGCT ATTCTTGTCG TGCTACCCGT GCACGGAAAA TCGATTGAGG 900
GAAGAACAAA TTTATCCGTG AAATCCACAG AGCGGATAAA TTTGTCACAT TGCTGCGTTG 960
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TTTTTTTGGT GTGTTGCTTT TTTGGCTGCT ACTTTCTACA ACCACCACCA CCACCACCAC 1140
CATGATTGAA CAAATCCTAG AATATTGGTA TATTGTTGTG CCTGTGTTGT ACATCATCAA 1200
ACAACTCATT GCCTACAGCA AGACTCGCGT CTTGATGAAA CAGTTGGGTG CTGCTCCAAT 1260
CACAAACCAG TTGTACGACA ACGTTTTCGG TATCGTCAAC GGATGGAAGG CTCTCCAGTT 1320
CAAGAAAGAG GGCAGAGCTC AAGAGTACAA CGATCACAAG TTTGACAGCT CCAAGAACCC 1380
AAGCGTCGGC ACCTATGTCA GTATTCTTTT TGGCACCAAG ATTGTCGTGA CCAAGGATCC 1440
AGAGAATATC AAAGCTATTT TGGCAACCCA GTTTGGCGAT TTTTCTTTGG GCAAGAGACA 1500
CGCTCTTTTT AAACCTTTGT TAGGTGATGG GATCTTCACC TTGGACGGCG AAGGCTGGAA 1560
GCATAGCAGA TCCATGTTAA GACCACAGTT TGCCAGAGAA CAAGTTGCTC ATGTGACGTC 1620
GTTGGAACCA CACTTCCAGT TGTTGAAGAA GCATATCCTT AAACACAAGG GTGAGTACTT 1680
TGATATCCAG GAATTGTTCT TTAGATTTAC TGTCGACTCG GCCACGGAGT TCTTATTTGG 1740
TGAGTCCGTG CACTCCTTAA AGGACGAAAC TATCGGTATC AACCAAGACG ATATAGATTT 1800
TGCTGGTAGA AAGGACTTTG CTGAGTCGTT CAACAAAGCC CAGGAGTATT TGTCTATTAG 1860
AATTTTGGTG CAGACCTTCT ACTGGTTGAT CAACAACAAG GAGTTTAGAG ACTGTACCAA 1920
GCTGGTGCAC AAGTTTACCA ACTACTATGT TCAGAAAGCT TTGGATGCTA CCCCAGAGGA 1980
ACTTGAAAAG CAAGGCGGGT ATGTGTTCTT GTATGAGCTT GTCAAGCAGA CGAGAGACCC 2040
CAAGGTGTTG CGTGACCAGT CTTTGAACAT CTTGTTGGCA GGAAGAGACA CCACTGCTGG 2100
GTTGTTGTCC TTTGCTGTGT TTGAGTTGGC CAGAAACCCA CACATCTGGG CCAAGTTGAG 2160
AGAGGAAATT GAACAGCAGT TTGGTCTTGG AGAAGACTCT CGTGTTGAAG AGATTACCTT 2220
TGAGAGCTTG AAGAGATGTG AGTACTTGAA AGCGTTCCTT AACGAAACCT TGCGTGTTTA 2280
CCCAAGTGTC CCAAGAAACT TCAGAATCGC CACCAAGAAT ACAACATTGC CAAGGGGTGG 2340
TGGTCCAGAC GGTACCCAGC CAATCTTGAT CCAAAAGGGA GAAGGTGTGT CGTATGGTAT 2400
CAACTCTACC CACTTAGATC CTGTCTATTA TGGCCCTGAT GCTGCTGAGT TCAGACCAGA 2460
GAGATGGTTT GAGCCATCAA CCAGAAAGCT CGGCTGGGCT TACTTGCCAT TCAACGGTGG 2520
GCCACGAATC TGTTTGGGTC AGCAGTTTGC CTTGACCGAA GCTGGTTACG TTTTGGTCAG 2580
ATTGGTGCAA GAGTTCTCCC ACATTAGGCT GGACCCAGAT GAAGTGTATC CACCAAAGAG 2640
GTTGACCAAC TTGACCATGT GTTTGCAGGA TGGTGCTATT GTCAAGTTTG ACTAGTACGT 2700

ATGAGTGCGT TTGATTTTGT AGTTTCTGTT TGCAGTAATG AGATAACTAT TCAGATAAGG 2760
CGGGTGGATG TACGTTTTGT AAGAGTTTCC TTACAACCCT GGTGGGTGTG TGAGGTTGCA 2820
TCTTAGGGAG AGATAGCACC TTTTGCAGCT CTCCGTATAC AGTTTTACTC TTTGTAACCT 2880
ATGCCAATCA TGTGGGGATT CATTGTTTGC CCATGGTGGT GCATGCAAAA TCCCCCCAAC 2940
TACCCAATCT CACATGAAAC TCAAGCACAC TAGAAAAAAA AGATGTTGCG TGGGTTCTTT 3000
TGATGTTGGG GAAAACTTTC GTTTCCTTTC TCAGTAATTA AACGTTCTCA CTCAGACAAA 3060
CCACCTGGGC TGCAGACAAC CAGAAAAAAC AAAATCCAGA TAGAAGAAGA AAGGGCTGGA 3120
CAACCATAAA TAAACAACCT AGGGTCCACT CCATCTTTCA CTTCTTCTTC TTCAGACTTA 3180
TCTAACAAAC GACTCACTTC ACCATGGATT ACGCAGGTAT CACGCGTGGG TCCATCAGAG 3240
GCGAAGCCTT GAAGAAACTC GCCGAGTTGA CCATCCAGAA CCAGCCATCC AGCTTGAAAG 3300
AAATCAACAC CGGCATCCAG AAGGACGACT TTGCCAAGTT GTTGTCTTCC ACCCCGAAAA 3360
TCCACACCAA GCACAAGTTG AATGGCAACC ACGAATTGTC CGAAGTCGCC ATTGCCAAAA 3420
AGGAGTACGA GGTGTTGATT GCCTTGAGCG ACGCCACGAA AGAACCAATC AAAGTCACCT 3480
CCCAGATCAA GATCTTGATT GACAAGTTCA AGGTGTACTT GTTTGAGTTG CCCGACCAGA 3540
AGTTCTCCTA CTCCATCGTG TCCAACTCCG TTAACATTGC CCCCTGGACC TTGCTCGGTG 3600
AGAAGTTGAC CACGGGCTTG ATCAACTTGG CGTTCCAGAA CAACAAGCAG CACTTGGACG 3660
AAGTCATCGA CATCTTCAAC GAGTTCATCG ACAAGTTCTT TGGCAACACA GAGCCGCAAT 3720
TGACCAACTT CTTGACCTTG TCCGGTGTGT TGGACGGGTT GATTGACCAT GCCAACTTCT 3780
TGAGCGTGTC CTCCAGGACC TTCAAGATCT TCTTGAACTT GGACTCGTTT GTGGACAACT 3840
CGGACTTCTT GAACGACGTG GAGAACTACT CCGACTTTTT GTACGACGAG CCGAACGAGT 3900
ACCAGAACTT 3910

(2) INFORMATION FOR SEQ ID NO:92:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3150 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA (genomic)
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

GAATTCTTTG GATCTAATTC CAGCTGATCT TGCTAATCCT TATCAACGTA GTTGTGATCA 60
TTGTTTGTCT GAATTATACA CACCAGTGGA AGAATATGGT CTAATTTGCA CGTCCCACTG 120
GCATTGTGTG TTTGTGGGGG GGGGGGGGTG CACACATTTT TAGTGCCATT CTTTGTTGAT 180
TACCCCTCCC CCCTATCATT CATTCCCACA GGATTAGTTT TTTCCTCACT GGAATTCGCT 240
GTCCACCTGT CAACCCCCCC CCCCCCCCCC CCCACTGCCC TACCCTGCCC TGCCCTGCAC 300
GTCCTGTGTT TTGTGCTGTG TCTTTCCCAC GCTATAAAAG CCCTGGCGTC CGGCCAAGGT 360
TTTTCCACCC AGCCAAAAAA ACAGTCTAAA AAATTTGGTT GATCCTTTTT GGTTGCAAGG 420
TTTTCCACCA CCACTTCCAC CACCTCAACT ATTCGAACAA AAGATGCTCG ATCAGATCTT 480
ACATTACTGG TACATTGTCT TGCCATTGTT GGCCATTATC AACCAGATCG TGGCTCATGT 540
CAGGACCAAT TATTTGATGA AGAAATTGGG TGCTAAGCCA TTCACACACG TCCAACGTGA 600
CGGGTGGTTG GGCTTCAAAT TCGGCCGTGA ATTCCTCAAA GCAAAAAGTG CTGGGAGACT 660
GGTTGATTTA ATCATCTCCC GTTTCCACGA TAATGAGGAC ACTTTCTCCA GCTATGCTTT 720
TGGCAACCAT GTGGTGTTCA CCAGGGACCC CGAGAATATC AAGGCGCTTT TGGCAACCCA 780
GTTTGGTGAT TTTTCATTGG GCAGCAGGGT CAAGTTCTTC AAACCATTAT TGGGGTACGG 840
TATCTTCACA TTGGACGCCG AAGGCTGGAA GCACAGCAGA GCCATGTTGA GACCACAGTT 900
TGCCAGAGAA CAAGTTGCTC ATGTGACGTC GTTGGAACCA CACTTCCAGT TGTTGAAGAA 960
GCATATCCTT AAACACAAGG GTGAGTACTT TGATATCCAG GAATTGTTCT TTAGATTTAC 1020
TGTCGACTCG GCCACGGAGT TCTTATTTGG TGAGTCCGTG CACTCCTTAA AGGACGAGGA 1080
AATTGGCTAC GACACGAAAG ACATGTCTGA AGAAAGACGC AGATTTGCCG ACGCGTTCAA 1140
CAAGTCGCAA GTCTACGTGG CCACCAGAGT TGCTTTACAG AACTTGTACT GGTTGGTCAA 1200
CAACAAAGAG TTCAAGGAGT GCAATGACAT TGTCCACAAG TTTACCAACT ACTATGTTCA 1260
GAAAGCCTTG GATGCTACCC CAGAGGAACT TGAAAAGCAA GGCGGGTATG TGTTCTTGTA 1320
TGAGCTTGTC AAGCAGACGA GAGACCCCAA GGTGTTGCGT GACCAGTCTT TGAACATCTT 1380
GTTGGCAGGA AGAGACACCA CTGCTGGGTT GTTGTCCTTT GCTGTGTTTG AGTTGGCCAG 1440
AAACCCACAC ATCTGGGCCA AGTTGAGAGA GGAAATTGAA CAGCAGTTTG GTCTTGGAGA 1500
AGACTCTCGT GTTGAAGAGA TTACCTTTGA GAGCTTGAAG AGATGTGAGT ACTTGAAGGC 1560

CGTGTTGAAC GAAACTTTGA GATTACACCC AAGTGTCCCA AGAAACGCAA GATTTGCGAT 1620
TAAAGACACG ACTTTACCAA GAGGCGGTGG CCCCAACGGC AAGGATCCTA TCTTGATCAG 1680
GAAGGATGAG GTGGTGCAGT ACTCCATCTC GGCAACTCAG ACAAATCCTG CTTATTATGG 1740
CGCCGATGCT GCTGATTTTA GACCGGAAAG ATGGTTTGAA CCATCAACTA GAAACTTGGG 1800
ATGGGCTTTC TTGCCATTCA ACGGTGGTCC AAGAATCTGT TTGGGACAAC AGTTTGCTTT 1860
GACTGAAGCC GGTTACGTTT TGGTTAGACT TGTTCAGGAG TTTCCAAACT TGTCACAAGA 1920
CCCCGAAACC AAGTACCCAC CACCTAGATT GGCACACTTG ACGATGTGCT TGTTTGACGG 1980
TGCACACGTC AAGATGTCAT AGGTTTCCCC ATACAAGTAG TTCAGTAATT ATACACTGTT 2040
TTTACTTTCT CTTCATACCA AATGGACAAA AGTTTTAAGC ATGCCTAACA ACGTGACCGG 2100
ACAATTGTGT CGCACTAGTA TGTAACAATT GTAAAAATAG TGTACACTAA TTTGTGGTGG 2160
CCGGAGATAA ATTACAGTTT GGTTTTGTGT AAACTCGCGG ATATCTCTGG CAGTTTCTCT 2220
TCTCCGCAGC AGCTTTGCCA CGGGTTTGCT CTGGGGCCAA CAAATTCAAA AGGGGGAGAA 2280
ACTTAACACC CCTTATCTCT CCACTCTAGG TTGTAGCTCT TGTGGGGATG CAATTGTCGT 2340
ACGTTTTTTA TGTTTTGTCT AGACTTTGAT GATTACGTTG GATTTCTTAT GTCTGAGGCG 2400
TGCTTGAAAG AAGTGTCAAA ATGTGACAGG CGACGCTATT CGACATGAAC GCGAAAGGGT 2460
TATTTGCATC AATACGAGGG GCTGACTCTA GTCTAGGATG GCAGTCCTAG GTTGCAAACA 2520
TGTTGCACCA TATCCCTCCT GGAGTTGGTC GACCTCGCCT ACGCCACCCT CAGCGATCGG 2580
CACTTTCCGT TGTTCAATAT TTCTCCTTCC CATTGTTCCA GGGGTTATCA ACAACGTTGC 2640
CGGCCTCCTC CCCAAATTAC AAGAAAAATA AATTGTCGCA CGGCACCGAT CTGTCAAAGA 2700
TACAGATAAA CCTTAAATCT GCAAAAACAA GACCCCTCCC CATAGCCTAG AAGCACCAGC 2760
AAGATGATGG AGCAACTCCT CCAGTACTGG TACATCGCAC TCTCTGTATG GTTCATCCTT 2820
CGCTACTTGG CTTCCCACGC ACGAGCCGTC TACTTGCGCC ACAAGCTCGG CGCGGCGCCA 2880
TTCACGCACA CCCAGTACGA CGGCTGGTAT GGGTTCAAGT TTGGGCGGGA GTTTCTCAAG 2940
GCGAAGAAGA TCGGGCGGCA GACGGACTTG GTGCATGCGC GGTTCCGTGG CGGCATGGAC 3000
ACCTTCTCGA GCTACACTTT CGGCATCCAT ATCATCCTTA CCCGGGACCC GGAGAACATC 3060
AAGGCGGTCT TGGCGACGCA GTTCGATGAC TTCTCGCTCG GTGGCAGGAT CAGGTTCTTG 3120
AAGCCGTTGT TGGGGTATGG GATATTCACG 3150

(2) INFORMATION FOR SEQ ID NO:93:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3579 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA (genomic)
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:

AAAACCGATA CAAGAAGAAG ACAGTCAACA AGAACGTTAA TGTCAACCAG GCGCCAAGAA 60
GACGGTTTGG CGGACTTGGA AGAATGTGGC ATTTGCCCAT GATGTTTATG TTCTGGAGAG 120
GTTTTTCAAG GAATCGTCAT CCTCCGCCAC CACAAGAACC ACCAGTTAAC GAGATCCATA 180
TTCACAACCC ACCGCAAGGT GACAATGCTC AACAACAACA GCAACAACAA CAACCCCCAC 240
AAGAACAGTG GAATAATGCC AGTCAACAAA GAGTGGTGAC AGACGAGGGA GAAAACGCAA 300
GCAACAGTGG TTCTGATGCA AGATCAGCTA CACCGCTTCA TCAGGAAAAG CAGGAGCTCC 360
CACCACCATA TGCCCATCAC GAGCAACACC AGCAGGTTAG TGTATAGTAG TCTGTAGTTA 420
AGTCAATGCA ATGTACCAAT AAGACTATCC CTTCTTACAA CCAAGTTTTC TGCCGCGCCT 480
GTCTGGCAAC AGATGCTGGC CGACACACTT TCAACTGAGT TTGGTCTAGA ATTCTTGCAC 540
ATGCACGACA AGGAAACTCT TACAAAGACA ACACTTGTGC TCTGATGCCA CTTGATCTTG 600
CTAAGCCTTA TCAACGTAAT TGAGATCATT GTTTGTCTGA ATTATACACA CCAGTGGAAG 660
AATCTGGTCT AATCTGCACG CCTCATGGGC ATTGTGTGTT TTGGGGGGGG GGGGGGGGGT 720
GCACACATTT TTAGTGCGAA TGTTTGTTTG CTGGTTCCCC CTCCCCCCTC CCCCCTATCA 780
TGCCCACAGG ATTAGTTTTT TCCTCACTGG AATTCGCTGT CCACCTGTCA ACCCCCTCAC 840
TGCCCTGCCC TGCCCTGCAC GCCCTGTGTT TTGTGCTGTG GCACTCCCAC GCTATAAAAG 900
CCCTGGCGTA CGGCCAAGGT TTTTCCTCAC AGCCAAAAAA AAATTTGGCT GATCCTTTTG 960
GGCTGCAAGG TTTTTCACCA CCACCACCAC CACCACCTCA ACTATTCAAA CAAAGGATGC 1020
TCGACCAGAT CTTCCATTAC TGGTACATTG TCTTGCCATT GTTGGTCATT ATCAAGCAGA 1080
TCGTGGCTCA TGCCAGGACC AATTATTTGA TGAAGAAGTT GGGCGCTAAG CCATTCACAC 1140
ATGTCCAACT AGACGGGTGG TTTGGCTTCA AATTTGGCCG TGAATTCCTC AAAGCTAAAA 1200

GTGCTGGGAG GCAGGTTGAT TTAATCATCT CCCGTTTCCA CGATAATGAG GACACTTTCT 1260
CCAGCTATGC TTTTGGCAAC CATGTGGTGT TCACCAGGGA CCCCGAGAAT ATCAAGGCGC 1320
TTTTGGCAAC CCAGTTTGGT GATTTTTCAT TGGGAAGCAG GGTCAAATTC TTCAAACCAT 1380
TGTTGGGGTA CGGTATCTTC ACCTTGGACG GCGAAGGCTG GAAGCACAGC AGAGCCATGT 1440
TGAGACCACA GTTTGCCAGA GAGCAAGTTG CTCATGTGAC GTCGTTGGAA CCACATTTCC 1500
AGTTGTTGAA GAAGCATATT CTTAAGCACA AGGGTGAATA CTTTGATATC CAGGAATTGT 1560
TCTTTAGATT TACCGTTGAT TCAGCGACGG AGTTCTTATT TGGTGAGTCC GTGCACTCCT 1620
TAAGGGACGA GGAAATTGGC TACGATACGA AGGACATGGC TGAAGAAAGA CGCAAATTTG 1680
CCGACGCGTT CAACAAGTCG CAAGTCTATT TGTCCACCAG AGTTGCTTTA CAGACATTGT 1740
ACTGGTTGGT CAACAACAAA GAGTTCAAGG AGTGCAACGA CATTGTCCAC AAGTTCACCA 1800
ACTACTATGT TCAGAAAGCC TTGGATGCTA CCCCAGAGGA ACTTGAAAAA CAAGGCGGGT 1860
ATGTGTTCTT GTACGAGCTT GCCAAGCAGA CGAAAGACCC CAATGTGTTG CGTGACCAGT 1920
CTTTGAACAT CTTGTTGGCT GGAAGGGACA CCACTGCTGG GTTGTTGTCC TTTGCTGTGT 1980
TTGAGTTGGC CAGGAACCCA CACATCTGGG CCAAGTTGAG AGAGGAAATT GAATCACACT 2040
TTGGGCTGGG TGAGGACTCT CGTGTTGAAG AGATTACCTT TGAGAGCTTG AAGAGATGTG 2100
AGTACTTGAA AGCCGTGTTG AACGAAACGT TGAGATTACA CCCAAGTGTC CCAAGAAACG 2160
CAAGATTTGC GATTAAAGAC ACGACTTTAC CAAGAGGCGG TGGCCCCAAC GGCAAGGATC 2220
CTATCTTGAT CAGAAAGAAT GAGGTGGTGC AATACTCCAT CTCGGCAACT CAGACAAATC 2280
CTGCTTATTA TGGCGCCGAT GCTGCTGATT TTAGACCGGA AAGATGGTTT GAGCCATCAA 2340
CTAGAAACTT GGGATGGGCT TACTTGCCAT TCAACGGTGG TCCAAGAATC TGCTTGGGAC 2400
AACAGTTTGC TTTGACCGAA GCCGGTTACG TTTTGGTTAG ACTTGTTCAG GAATTCCCTA 2460
GCTTGTCACA GGACCCCGAA ACTGAGTACC CACCACCTAG ATTGGCACAC TTGACGATGT 2520
GCTTGTTTGA CGGGGCATAC GTCAAGATGC AATAGGTTTT GGTTTGACTT TGTTTCCATA 2580
TGCAAGTAGT TCAGTAATTA CACACTAATT TGTGGTGGCC GGCGATAAAT TACCGTTTGG 2640
TTTTGTGTAA AAATTCGGAC ATCTCTGGTG GTTTCCCTTC TCCGCAGCAG CTTTGCCACG 2700
GGTTTGCTCT GCGGCCAACA AATTCGAAAG GGGGGGGGGG GGGGGAGAAA GTTAACACCC 2760
CCTGTTCCCA CCGTAGGCTG TAGCTCTTGT GGGGGGATGT AATTGTCGTA CGTTTTCATG 2820
TTTGGCCCAG ACTTTGATGA TTACGTAGGC TTTCTTATGT CTAAGGCGTG CTTGACACAA 2880
GTGTCAAAAG GTGACAGGCG ACGTTATTCG ACATGAACGC AAAAGGGTAA TTTGCATCGA 2940
TACGAGGGGT TGCCTCTGGT CTAAGAAGGA CCCCCCAGGT TGCAAACATG TTGCACTGCA 3000
TCCCACTCAG AGTTGGTCGA CCACGCCTAC GCTTACCCTC AGCGATCGGC ACTTTCCGTT 3060
GCTCAATATT TCTCTCCCCC CTGCTTCCCC CCATTGTTCC AGGGATTATC AACAACGTTG 3120
CCGGTCTCCT CTCCCCCCCC TCCCCCCAGT TATGTACAAG AAAATTAAAT TGTCGCACGG 3180
CACCGATACG TCAAAGATAC AGAGAAACCT TAATCCCTCC CATAGCCTAG AAGCATCAAA 3240
AAGATGATTG AGCAACTCCT CCAGTACTGG TACATTGCAC TCCCTGTATG GTTCATTCTC 3300
CGCTACGTGG CTTCCCACGC ACGAACCATC TACTTGCGCC ACAAGCTCGG CGCGGCGCCG 3360
TTCACGCACA CCCAGTACGA CGGATGGTAT GGGTTCAAGT TTGGGCGGGA GTTTCTCAAG 3420
GCGAAGAAGA TTGGAAGGCA GACGGACTTG GTGCATGCGC GGTTCCGTGG AGGGGGCATG 3480
GATACTTTCT CGAGCTATAC TTTCGGCATC CATATCATTC TTACTCGGGA CCCGGAGAAC 3540
ATCAAGGCGG TCTTGGCGAC GCAGTTCGAT GACTTTTCG 3579

(2) INFORMATION FOR SEQ ID NO:94:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3348 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA (genomic)
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:

GATGTGGTGC TTGATTTCTC GAGACACATC CTTGTGAGGT GCCATGAATC TGTACCTGTC 60
TGTAAGCACA GGGAACTGCT TCAACACCTT ATTGCATATT CTGTCTATTG CAAGCGTGTG 120
CTGCAACGAT ATCTGCCAAG GTATATAGCA GAACGTGCTG ATGGTTCCTC CGGTCATATT 180
CTGTTGGTAG TTCTGCAGGT AAATTTGGAT GTCAGGTAGT GGAGGGAGGT TTGTATCGGT 240
TGTGTTTTCT TCTTCCTCTC TCTCTGATTC AACCTCCACG TCTCCTTCGG GTTCTGTGTC 300
TGTGTCTGAG TCGTACTGTT GGATTAAGTC CATCGCATGT GTGAAAAAAA GTAGCGCTTA 360
TTTAGACAAC CAGTTCGTTG GGCGGGTATC AGAAATAGTC TGTTGTGCAC GACCATGAGT 420

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ATGCAACTTG ACGAGACGTC GTTAGGAATC CACAGAATGA TAGCAGGAAG CTTACTACGT     480
GAGAGATTCT GCTTAGAGGA TGTTCTCTTC TTGTTGATTC CATTAGGTGG GTATCATCTC     540
CGGTGGTGAC AACTTGACAC AAGCAGTTCC GAGAACCACC CACAACAATC ACCATTCCAG     600
CTATCACTTC TACATGTCAA CCTACGATGT ATCTCATCAC CATCTAGTTT CTTGGCAATC     660
GTTTATTTGT TATGGGTCAA CATCCAATAC AACTCCACCA ATGAAGAAGA AAAACGGAAA     720
GCAGAATACC AGAATGACAG TGTGAGTTCC TGACCATTGC TAATCTATGG CTATATCTAG     780
TTTGCTATCG TGGGATGTGA TCTGTGTCGT CTTCATTTGC GTTTGTGTTT ATTTCGGGTA     840
TGAATATTGT TATACTAAAT ACTTGATGCA CAAACATGGC GCTCGAGAAA TCGAGAATGT     900
GATCAACGAT GGGTTCTTTG GGTTCCGCTT ACCTTTGCTA CTCATGCGAG CCAGCAATGA     960
GGGCCGACTT ATCGAGTTCA GTGTCAAGAG ATTCGAGTCG GCGCCACATC CACAGAACAA    1020
GACATTGGTC AACCGGGCAT TGAGCGTTCC TGTGATACTC ACCAAGGACC CAGTGAATAT    1080
CAAAGCGATG CTATCGACCC AGTTTGATGA CTTTTCCCTT GGGTTGAGAC TACACCAGTT    1140
TGCGCCGTTG TTGGGGAAAG GCATCTTTAC TTTGGACGGC CCAGAGTGGA AGCAGAGCCG    1200
ATCTATGTTG CGTCCGCAAT TTGCCAAAGA TCGGGTTTCT CATATCCTGG ATCTAGAACC    1260
GCATTTTGTG TTGCTTCGGA AGCACATTGA TGGCCACAAT GGAGACTACT TCGACATCCA    1320
GGAGCTCTAC TTCCGGTTCT CGATGGATGT GGCGACGGGG TTTTTGTTTG GCGAGTCTGT    1380
GGGGTCGTTG AAAGACGAAG ATGCGAGGTT CCTGGAAGCA TTCAATGAGT CGCAGAAGTA    1440
TTTGGCAACT AGGGCAACGT TGCACGAGTT GTACTTTCTT TGTGACGGGT TTAGGTTTCG    1500
CCAGTACAAC AAGGTTGTGC GAAAGTTCTG CAGCCAGTGT GTCCACAAGG CGTTAGATGT    1560
TGCACCGGAA GACACCAGCG AGTACGTGTT TCTCCGCGAG TTGGTCAAAC ACACTCGAGA    1620
TCCCGTTGTT TTACAAGACC AAGCGTTGAA CGTCTTGCTT GCTGGACGCG ACACCACCGC    1680
GTCGTTATTA TCGTTTGCAA CATTTGAGCT AGCCCGGAAT GACCACATGT GGAGGAAGCT    1740
ACGAGAGGAG GTTATCCTGA CGATGGGACC GTCCAGTGAT GAAATAACCG TGGCCGGGTT    1800
GAAGAGTTGC CGTTACCTCA AAGCAATCCT AAACGAAACT CTTCGACTAT ACCCAAGTGT    1860
GCCTAGGAAC GCGAGATTTG CTACGAGGAA TACGACGCTT CCTCGTGGCG GAGGTCCAGA    1920
TGGATCGTTT CCGATTTTGA TAAGAAAGGG CCAGCCAGTG GGGTATTTCA TTTGTGCTAC    1980
ACACTTGAAT GAGAAGGTAT ATGGGAATGA TAGCCATGTG TTTCGACCGG AGAGATGGGC    2040
TGCGTTAGAG GGCAAGAGTT TGGGCTGGTC GTATCTTCCA TTCAACGGCG GCCCGAGAAG    2100
CTGCCTTGGT CAGCAGTTTG CAATCCTTGA AGCTTCGTAT GTTTTGGCTC GATTGACACA    2160
GTGCTACACG ACGATACAGC TTAGAACTAC CGAGTACCCA CCAAAGAAAC TCGTTCATCT    2220
CACGATGAGT CTTCTCAACG GGGTGTACAT CCGAACTAGA ACTTGATTAT GTGTTTATGG    2280
TTAATCGGGG CAAAGCACTG CAAGTCATTG ATGTTTGTGG AAGCCCAGCA TTGGTGTTCC    2340
GGAGCATCAA TAACCAATGT CTTGAAGGGT TTGATTTTCT TGACCTTCTT CTTCCTGAGC    2400
TTCTTTCCGT CAAACTTGTA CAGAATGGCC ATCATTTCAG GAACAACCAC GTACGACGGC    2460
CGGTACCGCA TCTGGAGTAT CTCGCCGTCG TTCAAGTAGC ACGAAAACAG CAACGACGTC    2520
ACCATCTGCT TCCCAATCTT GACACCCACA GATACCCCTG CGGCTTCATG GATCAAAAAC    2580
GTCGGCAACC CCGCGTATAT GTCCATGTAA TTCTCCATGG CCACCTCCAT CAACACACTG    2640
ATGGAGCGAC TGACGGTGCC ACCACTGCCC TCGGTTGAGT CAAGGCAGTA TGATGCCGGG    2700
ATCCAGTACT CCAATGGGAA CCTCTGCACG GTGTCGCTGC AGTTTTTGAG GCGTATTTCG    2760
ATCCATGATC GTTCTTTGGT GCTGTAGTAT AACGAGCTCT TGGTGTCCTT GAAATGGAAC    2820
AGGTTGGATG TGTTGTTGAG TTTGTCTGCG TGCTTGGTTT GCAAGTCTTC GATCGAGCGT    2880
AGTGAGTAGA CAGTTGGCGG GGGTGGTGGC TCGGGCTTTA TTCTGTGTTT GTGTTTCCTT    2940
CTTAGTCTTG GAATGACGCT GTTATCGACG GTTCGTAGTA TAAGTAGCGC CAATATGAGA    3000
ATGTATATCC GCATCACCCA AGACTCTTCA GCCTGTTACA ACGACTGAGG CTGTTGGCCG    3060
TGTGACCAAT TGGTTTCTTT GGTGACCTAG ATTGGTCCCG CAGGGAAAGC AAGGGCTGCT    3120
AGGGGGGCAT ACCAAACAAG GTCGTGTAAT CAGTATCTAT GGTGCTACCA TGTGTGTGGT    3180
TGGGGGGAAA TTCCCGCATT TTTGTGTAAC GAAAGTTCTA GAAAGTTCTC GTGGGTTCTG    3240
AGAATCTGCT GGAACCATCC ACCCGCATTT CCGTTGCCAA AGTGGGAAGA GCAATCAACC    3300
CACCCTGCTT TGCCCAATCA GCCATTCCCC TGGGAATATA AATTCAAC                  3348
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(2) INFORMATION FOR SEQ ID NO:95:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 523 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

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Met Ala Thr Gln Glu Ile Ile Asp Ser Val Leu Pro Tyr Leu Thr Lys
1               5                  10                  15
Trp Tyr Thr Val Ile Thr Ala Ala Val Leu Val Phe Leu Ile Ser Thr
            20                  25                  30
Asn Ile Lys Asn Tyr Val Lys Ala Lys Lys Leu Lys Cys Val Asp Pro
        35                  40                  45
Pro Tyr Leu Lys Asp Ala Gly Leu Thr Gly Ile Leu Ser Leu Ile Ala
    50                  55                  60
Ala Ile Lys Ala Lys Asn Asp Gly Arg Leu Ala Asn Phe Ala Asp Glu
65                  70                  75                  80
Val Phe Asp Glu Tyr Pro Asn His Thr Phe Tyr Leu Ser Val Ala Gly
                85                  90                  95
Ala Leu Lys Ile Val Met Thr Val Asp Pro Glu Asn Ile Lys Ala Val
            100                 105                 110
Leu Ala Thr Gln Phe Thr Asp Phe Ser Leu Gly Thr Arg His Ala His
        115                 120                 125
Phe Ala Pro Leu Leu Gly Asp Gly Ile Phe Thr Leu Asp Gly Glu Gly
    130                 135                 140
Trp Lys His Ser Arg Ala Met Leu Arg Pro Gln Phe Ala Arg Asp Gln
145                 150                 155                 160
Ile Gly His Val Lys Ala Leu Glu Pro His Ile Gln Ile Met Ala Lys
                165                 170                 175
Gln Ile Lys Leu Asn Gln Gly Lys Thr Phe Asp Ile Gln Glu Leu Phe
            180                 185                 190
Phe Arg Phe Thr Val Asp Thr Ala Thr Glu Phe Leu Phe Gly Glu Ser
        195                 200                 205
Val His Ser Leu Tyr Asp Glu Lys Leu Gly Ile Pro Thr Pro Asn Glu
    210                 215                 220
Ile Pro Gly Arg Glu Asn Phe Ala Ala Ala Phe Asn Val Ser Gln His
225                 230                 235                 240
Tyr Leu Ala Thr Arg Ser Tyr Ser Gln Thr Phe Tyr Phe Leu Thr Asn
                245                 250                 255
Pro Lys Glu Phe Arg Asp Cys Asn Ala Lys Val His His Leu Ala Lys
            260                 265                 270
Tyr Phe Val Asn Lys Ala Leu Asn Phe Thr Pro Glu Glu Leu Glu Glu
        275                 280                 285
Lys Ser Lys Ser Gly Tyr Val Phe Leu Tyr Glu Leu Val Lys Gln Thr
    290                 295                 300
Arg Asp Pro Lys Val Leu Gln Asp Gln Leu Leu Asn Ile Met Val Ala
305                 310                 315                 320
Gly Arg Asp Thr Thr Ala Gly Leu Leu Ser Phe Ala Leu Phe Glu Leu
                325                 330                 335
Ala Arg His Pro Glu Met Trp Ser Lys Leu Arg Glu Glu Ile Glu Val
            340                 345                 350
Asn Phe Gly Val Gly Glu Asp Ser Arg Val Glu Glu Ile Thr Phe Glu
        355                 360                 365
Ala Leu Lys Arg Cys Glu Tyr Leu Lys Ala Ile Leu Asn Glu Thr Leu
    370                 375                 380
Arg Met Tyr Pro Ser Val Pro Val Asn Phe Arg Thr Ala Thr Arg Asp
385                 390                 395                 400
Thr Thr Leu Pro Arg Gly Gly Gly Ala Asn Gly Thr Asp Pro Ile Tyr
                405                 410                 415
Ile Pro Lys Gly Ser Thr Val Ala Tyr Val Val Tyr Lys Thr His Arg
            420                 425                 430
```

```
Leu Glu Glu Tyr Tyr Gly Lys Asp Ala Asn Asp Phe Arg Pro Glu Arg
        435                 440                 445
Trp Phe Glu Pro Ser Thr Lys Lys Leu Gly Trp Ala Tyr Val Pro Phe
    450                 455                 460
Asn Gly Gly Pro Arg Val Cys Leu Gly Gln Gln Phe Ala Leu Thr Glu
465                 470                 475                 480

Ala Ser Tyr Val Ile Thr Arg Leu Ala Gln Met Phe Glu Thr Val Ser
                485                 490                 495
Ser Asp Pro Gly Leu Glu Tyr Pro Pro Pro Lys Cys Ile His Leu Thr
            500                 505                 510
Met Ser His Asn Asp Gly Val Phe Val Lys Met
        515                 520
```

(2) INFORMATION FOR SEQ ID NO:96:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 522 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

```
Met Thr Val His Asp Ile Ile Ala Thr Tyr Phe Thr Lys Trp Tyr Val
1               5                  10                  15
Ile Val Pro Leu Ala Leu Ile Ala Tyr Arg Val Leu Asp Tyr Phe Tyr
            20                  25                  30
Gly Arg Tyr Leu Met Tyr Lys Leu Gly Ala Lys Pro Phe Phe Gln Lys
        35                  40                  45
Gln Thr Asp Gly Cys Phe Gly Phe Lys Ala Pro Leu Glu Leu Leu Lys
    50                  55                  60
Lys Lys Ser Asp Gly Thr Leu Ile Asp Phe Thr Leu Gln Arg Ile His
65                  70                  75                  80
Asp Leu Asp Arg Pro Asp Ile Pro Thr Phe Thr Phe Pro Val Phe Ser
                85                  90                  95
Ile Asn Leu Val Asn Thr Leu Glu Pro Glu Asn Ile Lys Ala Ile Leu
            100                 105                 110
Ala Thr Gln Phe Asn Asp Phe Ser Leu Gly Thr Arg His Ser His Phe
        115                 120                 125
Ala Pro Leu Leu Gly Asp Gly Ile Phe Thr Leu Asp Gly Ala Gly Trp
    130                 135                 140
Lys His Ser Arg Ser Met Leu Arg Pro Gln Phe Ala Arg Glu Gln Ile
145                 150                 155                 160
Ser His Val Lys Leu Leu Glu Pro His Val Gln Val Phe Phe Lys His
                165                 170                 175
Val Arg Lys Ala Gln Gly Lys Thr Phe Asp Ile Gln Glu Leu Phe Phe
            180                 185                 190
Arg Leu Thr Val Asp Ser Ala Thr Glu Phe Leu Phe Gly Glu Ser Val
        195                 200                 205
Glu Ser Leu Arg Asp Glu Ser Ile Gly Met Ser Ile Asn Ala Leu Asp
    210                 215                 220
Phe Asp Gly Lys Ala Gly Phe Ala Asp Ala Phe Asn Tyr Ser Gln Asn
225                 230                 235                 240
Tyr Leu Ala Ser Arg Ala Val Met Gln Gln Leu Tyr Trp Val Leu Asn
                245                 250                 255
Gly Lys Lys Phe Lys Glu Cys Asn Ala Lys Val His Lys Phe Ala Asp
            260                 265                 270
```

```
Tyr Tyr Val Asn Lys Ala Leu Asp Leu Thr Pro Glu Gln Leu Glu Lys
        275                 280                 285
Gln Asp Gly Tyr Val Phe Leu Tyr Glu Leu Val Lys Gln Thr Arg Asp
    290                 295                 300
Lys Gln Val Leu Arg Asp Gln Leu Leu Asn Ile Met Val Ala Gly Arg
305                 310                 315                 320

Asp Thr Thr Ala Gly Leu Leu Ser Phe Val Phe Phe Glu Leu Ala Arg
                325                 330                 335
Asn Pro Glu Val Thr Asn Lys Leu Arg Glu Glu Ile Glu Asp Lys Phe
            340                 345                 350
Gly Leu Gly Glu Asn Ala Ser Val Glu Asp Ile Ser Phe Glu Ser Leu
        355                 360                 365
Lys Ser Cys Glu Tyr Leu Lys Ala Val Leu Asn Glu Thr Leu Arg Leu
    370                 375                 380
Tyr Pro Ser Val Pro Gln Asn Phe Arg Val Ala Thr Lys Asn Thr Thr
385                 390                 395                 400
Leu Pro Arg Gly Gly Gly Lys Asp Gly Leu Ser Pro Val Leu Val Arg
                405                 410                 415
Lys Gly Gln Thr Val Ile Tyr Gly Val Tyr Ala Ala His Arg Asn Pro
            420                 425                 430
Ala Val Tyr Gly Lys Asp Ala Leu Glu Phe Arg Pro Glu Arg Trp Phe
        435                 440                 445
Glu Pro Glu Thr Lys Lys Leu Gly Trp Ala Phe Leu Pro Phe Asn Gly
    450                 455                 460
Gly Pro Arg Ile Cys Leu Gly Gln Gln Phe Ala Leu Thr Glu Ala Ser
465                 470                 475                 480
Tyr Val Thr Val Arg Leu Leu Gln Glu Phe Ala His Leu Ser Met Asp
                485                 490                 495
Pro Asp Thr Glu Tyr Pro Pro Lys Lys Met Ser His Leu Thr Met Ser
            500                 505                 510
Leu Phe Asp Gly Ala Asn Ile Glu Met Tyr
        515                 520
```

(2) INFORMATION FOR SEQ ID NO:97:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 522 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:

```
Met Thr Ala Gln Asp Ile Ile Ala Thr Tyr Ile Thr Lys Trp Tyr Val
1               5                   10                  15
Ile Val Pro Leu Ala Leu Ile Ala Tyr Arg Val Leu Asp Tyr Phe Tyr
            20                  25                  30
Gly Arg Tyr Leu Met Tyr Lys Leu Gly Ala Lys Pro Phe Phe Gln Lys
        35                  40                  45
Gln Thr Asp Gly Tyr Phe Gly Phe Lys Ala Pro Leu Glu Leu Leu Lys
    50                  55                  60
Lys Lys Ser Asp Gly Thr Leu Ile Asp Phe Thr Leu Glu Arg Ile Gln
65                  70                  75                  80
Ala Leu Asn Arg Pro Asp Ile Pro Thr Phe Thr Phe Pro Ile Phe Ser
                85                  90                  95
Ile Asn Leu Ile Ser Thr Leu Glu Pro Glu Asn Ile Lys Ala Ile Leu
            100                 105                 110
```

```
Ala Thr Gln Phe Asn Asp Phe Ser Leu Gly Thr Arg His Ser His Phe
        115                 120                 125
Ala Pro L u Leu Gly Asp Gly Ile Phe Thr Leu Asp Gly Ala Gly Trp
    130                 135                 140
Lys His Ser Arg Ser Met Leu Arg Pro Gln Phe Ala Arg Glu Gln Ile
145                 150                 155                 160
Ser His Val Lys Leu Leu Glu Pro His Met Gln Val Phe Phe Lys His
                165                 170                 175
Val Arg Lys Ala Gln Gly Lys Thr Phe Asp Ile Gln Glu Leu Phe Phe
            180                 185                 190
Arg Leu Thr Val Asp Ser Ala Thr Glu Phe Leu Phe Gly Glu Ser Val
        195                 200                 205
Glu Ser Leu Arg Asp Glu Ser Ile Gly Met Ser Ile Asn Ala Leu Asp
    210                 215                 220
Phe Asp Gly Lys Ala Gly Phe Ala Asp Ala Phe Asn Tyr Ser Gln Asn
225                 230                 235                 240
Tyr Leu Ala Ser Arg Ala Val Met Gln Gln Leu Tyr Trp Val Leu Asn
                245                 250                 255
Gly Lys Lys Phe Lys Glu Cys Asn Ala Lys Val His Lys Phe Ala Asp
            260                 265                 270
Tyr Tyr Val Ser Lys Ala Leu Asp Leu Thr Pro Glu Gln Leu Glu Lys
        275                 280                 285
Gln Asp Gly Tyr Val Phe Leu Tyr Glu Leu Val Lys Gln Thr Arg Asp
    290                 295                 300
Arg Gln Val Leu Arg Asp Gln Leu Leu Asn Ile Met Val Ala Gly Arg
305                 310                 315                 320
Asp Thr Thr Ala Gly Leu Leu Ser Phe Val Phe Phe Glu Leu Ala Arg
                325                 330                 335
Asn Pro Glu Val Thr Asn Lys Leu Arg Glu Glu Ile Glu Asp Lys Phe
            340                 345                 350
Gly Leu Gly Glu Asn Ala Arg Val Glu Asp Ile Ser Phe Glu Ser Leu
        355                 360                 365
Lys Ser Cys Glu Tyr Leu Lys Ala Val Leu Asn Glu Thr Leu Arg Leu
    370                 375                 380
Tyr Pro Ser Val Pro Gln Asn Phe Arg Val Ala Thr Lys Asn Thr Thr
385                 390                 395                 400
Leu Pro Arg Gly Gly Gly Lys Asp Gly Leu Ser Pro Val Leu Val Arg
                405                 410                 415
Lys Gly Gln Thr Val Met Tyr Gly Val Tyr Ala Ala His Arg Asn Pro
            420                 425                 430
Ala Val Tyr Gly Lys Asp Ala Leu Glu Phe Arg Pro Glu Arg Trp Phe
        435                 440                 445
Glu Pro Glu Thr Lys Lys Leu Gly Trp Ala Phe Leu Pro Phe Asn Gly
    450                 455                 460
Gly Pro Arg Ile Cys Leu Gly Gln Gln Phe Ala Leu Thr Glu Ala Ser
465                 470                 475                 480
Tyr Val Thr Val Arg Leu Leu Gln Glu Phe Gly His Leu Ser Met Asp
                485                 490                 495
Pro Asn Thr Glu Tyr Pro Pro Arg Lys Met Ser His Leu Thr Met Ser
            500                 505                 510
Leu Phe Asp Gly Ala Asn Ile Glu Met Tyr
        515                 520
```

(2) INFORMATION FOR SEQ ID NO:98:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 540 amino acids

(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

```
Met Ser Ser Ser Pro Ser Phe Ala Gln Glu Val Leu Ala Thr Thr Ser
1               5                  10                  15
Pro Tyr Ile Glu Tyr Phe Leu Asp Asn Tyr Thr Arg Trp Tyr Tyr Phe
            20                  25                  30
Ile Pro Leu Val Leu Leu Ser Leu Asn Phe Ile Ser Leu Leu His Thr
        35                  40                  45
Arg Tyr Leu Glu Arg Arg Phe His Ala Lys Pro Leu Gly Asn Phe Val
    50                  55                  60
Arg Asp Pro Thr Phe Gly Ile Ala Thr Pro Leu Leu Leu Ile Tyr Leu
65                  70                  75                  80
Lys Ser Lys Gly Thr Val Met Lys Phe Ala Trp Gly Leu Trp Asn Asn
                85                  90                  95
Lys Tyr Ile Val Arg Asp Pro Lys Tyr Lys Thr Thr Gly Leu Arg Ile
            100                 105                 110
Val Gly Leu Pro Leu Ile Glu Thr Met Asp Pro Glu Asn Ile Lys Ala
        115                 120                 125
Val Leu Ala Thr Gln Phe Asn Asp Phe Ser Leu Gly Thr Arg His Asp
    130                 135                 140
Phe Leu Tyr Ser Leu Leu Gly Asp Gly Ile Phe Thr Leu Asp Gly Ala
145                 150                 155                 160
Gly Trp Lys His Ser Arg Thr Met Leu Arg Pro Gln Phe Ala Arg Glu
                165                 170                 175
Gln Val Ser His Val Lys Leu Leu Glu Pro His Val Gln Val Phe Phe
            180                 185                 190
Lys His Val Arg Lys His Arg Gly Gln Thr Phe Asp Ile Gln Glu Leu
        195                 200                 205
Phe Phe Arg Leu Thr Val Asp Ser Ala Thr Glu Phe Leu Phe Gly Glu
    210                 215                 220
Ser Ala Glu Ser Leu Arg Asp Glu Ser Ile Gly Leu Thr Pro Thr Thr
225                 230                 235                 240
Lys Asp Phe Asp Gly Arg Arg Asp Phe Ala Asp Ala Phe Asn Tyr Ser
                245                 250                 255
Gln Thr Tyr Gln Ala Tyr Arg Phe Leu Leu Gln Gln Met Tyr Trp Ile
            260                 265                 270
Leu Asn Gly Ser Glu Phe Arg Lys Ser Ile Ala Val Val His Lys Phe
        275                 280                 285
Ala Asp His Tyr Val Gln Lys Ala Leu Glu Leu Thr Asp Asp Asp Leu
    290                 295                 300
Gln Lys Gln Asp Gly Tyr Val Phe Leu Tyr Glu Leu Ala Lys Gln Thr
305                 310                 315                 320
Arg Asp Pro Lys Val Leu Arg Asp Gln Leu Leu Asn Ile Leu Val Ala
                325                 330                 335
Gly Arg Asp Thr Thr Ala Gly Leu Leu Ser Phe Val Phe Tyr Glu Leu
            340                 345                 350
Ser Arg Asn Pro Glu Val Phe Ala Lys Leu Arg Glu Glu Val Glu Asn
        355                 360                 365
Arg Phe Gly Leu Gly Glu Glu Ala Arg Val Glu Glu Ile Ser Phe Glu
    370                 375                 380
Ser Leu Lys Ser Cys Glu Tyr Leu Lys Ala Val Ile Asn Glu Thr Leu
385                 390                 395                 400
```

```
Arg Leu Tyr Pro Ser Val Pro His Asn Phe Arg Val Ala Thr Arg Asn
                405                 410                 415
Thr Thr Leu Pro Arg Gly Gly Gly Glu Asp Gly Tyr Ser Pr  Ile Val
            420                 425                 430
Val Lys Lys Gly Gln Val Val Met Tyr Thr Val Ile Ala Thr His Arg
        435                 440                 445
Asp Pro Ser Ile Tyr Gly Ala Asp Ala Asp Val Phe Arg Pro Glu Arg
    450                 455                 460
Trp Phe Glu Pro Glu Thr Arg Lys Leu Gly Trp Ala Tyr Val Pro Phe
465                 470                 475                 480
Asn Gly Gly Pro Arg Ile Cys Leu Gly Gln Gln Phe Ala Leu Thr Glu
                485                 490                 495
Ala Ser Tyr Val Thr Val Arg Leu Leu Gln Glu Phe Ala His Leu Ser
            500                 505                 510
Met Asp Pro Asp Thr Glu Tyr Pro Pro Lys Leu Gln Asn Thr Leu Thr
        515                 520                 525
Leu Ser Leu Phe Asp Gly Ala Asp Val Arg Met Tyr
    530                 535                 540
```

(2) INFORMATION FOR SEQ ID NO:99:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 540 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:

```
Met Ser Ser Ser Pro Ser Phe Ala Gln Glu Val Leu Ala Thr Thr Ser
1               5                   10                  15
Pro Tyr Ile Glu Tyr Phe Leu Asp Asn Tyr Thr Arg Trp Tyr Tyr Phe
            20                  25                  30
Ile Pro Leu Val Leu Leu Ser Leu Asn Phe Ile Ser Leu Leu His Thr
        35                  40                  45
Lys Tyr Leu Glu Arg Arg Phe His Ala Lys Pro Leu Gly Asn Val Val
    50                  55                  60
Leu Asp Pro Thr Phe Gly Ile Ala Thr Pro Leu Ile Leu Ile Tyr Leu
65                  70                  75                  80
Lys Ser Lys Gly Thr Val Met Lys Phe Ala Trp Ser Phe Trp Asn Asn
                85                  90                  95
Lys Tyr Ile Val Lys Asp Pro Lys Tyr Lys Thr Thr Gly Leu Arg Ile
            100                 105                 110
Val Gly Leu Pro Leu Ile Glu Thr Ile Asp Pro Glu Asn Ile Lys Ala
        115                 120                 125
Val Leu Ala Thr Gln Phe Asn Asp Phe Ser Leu Gly Thr Arg His Asp
    130                 135                 140
Phe Leu Tyr Ser Leu Leu Gly Asp Gly Ile Phe Thr Leu Asp Gly Ala
145                 150                 155                 160
Gly Trp Lys His Ser Arg Thr Met Leu Arg Pro Gln Phe Ala Arg Glu
                165                 170                 175
Gln Val Ser His Val Lys Leu Leu Glu Pro His Val Gln Val Phe Phe
            180                 185                 190
Lys His Val Arg Lys His Arg Gly Gln Thr Phe Asp Ile Gln Glu Leu
        195                 200                 205
Phe Phe Arg Leu Thr Val Asp Ser Ala Thr Glu Phe Leu Phe Gly Glu
    210                 215                 220
```

```
Ser Ala Glu Ser Leu Arg Asp Asp Ser Val Gly Leu Thr Pro Thr Thr
225                 230                 235                 240
Lys Asp Phe Glu Gly Arg Gly Asp Phe Ala Asp Ala Phe Asn Tyr Ser
                245                 250                 255
Gln Thr Tyr Gln Ala Tyr Arg Phe Leu Leu Gln Gln Met Tyr Trp Ile
            260                 265                 270
Leu Asn Gly Ala Glu Phe Arg Lys Ser Ile Ala Ile Val His Lys Phe
        275                 280                 285
Ala Asp His Tyr Val Gln Lys Ala Leu Glu Leu Thr Asp Asp Asp Leu
    290                 295                 300
Gln Lys Gln Asp Gly Tyr Val Phe Leu Tyr Glu Leu Ala Lys Gln Thr
305                 310                 315                 320
Arg Asp Pro Lys Val Leu Arg Asp Gln Leu Leu Asn Ile Leu Val Ala
                325                 330                 335
Gly Arg Asp Thr Thr Ala Gly Leu Leu Ser Phe Val Phe Tyr Glu Leu
            340                 345                 350
Ser Arg Asn Pro Glu Val Phe Ala Lys Leu Arg Glu Glu Val Glu Asn
        355                 360                 365
Arg Phe Gly Leu Gly Glu Glu Ala Arg Val Glu Glu Ile Ser Phe Glu
    370                 375                 380
Ser Leu Lys Ser Cys Glu Tyr Leu Lys Ala Val Ile Asn Glu Ala Leu
385                 390                 395                 400
Arg Leu Tyr Pro Ser Val Pro His Asn Phe Arg Val Ala Thr Arg Asn
                405                 410                 415
Thr Thr Leu Pro Arg Gly Gly Gly Lys Asp Gly Cys Ser Pro Ile Val
            420                 425                 430
Val Lys Lys Gly Gln Val Val Met Tyr Thr Val Ile Gly Thr His Arg
        435                 440                 445
Asp Pro Ser Ile Tyr Gly Ala Asp Ala Asp Val Phe Arg Pro Glu Arg
    450                 455                 460
Trp Phe Glu Pro Glu Thr Arg Lys Leu Gly Trp Ala Tyr Val Pro Phe
465                 470                 475                 480
Asn Gly Gly Pro Arg Ile Cys Leu Gly Gln Gln Phe Ala Leu Thr Glu
                485                 490                 495
Ala Ser Tyr Val Thr Val Arg Leu Leu Gln Glu Phe Gly Asn Leu Ser
            500                 505                 510
Leu Asp Pro Asn Ala Glu Tyr Pro Pro Lys Leu Gln Asn Thr Leu Thr
        515                 520                 525
Leu Ser Leu Phe Asp Gly Ala Asp Val Arg Met Phe
    530                 535                 540
```

(2) INFORMATION FOR SEQ ID NO:100:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 517 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

```
Met Ile Glu Gln Leu Leu Glu Tyr Trp Tyr Val Val Val Pro Val Leu
1               5                   10                  15
Tyr Ile Ile Lys Gln Leu Leu Ala Tyr Thr Lys Thr Arg Val Leu Met
            20                  25                  30
Lys Lys Leu Gly Ala Ala Pro Val Thr Asn Lys Leu Tyr Asp Asn Ala
        35                  40                  45
```

```
Phe Gly Ile Val Asn Gly Trp Lys Ala Leu Gln Phe Lys Lys Glu Gly
    50                  55                  60
Arg Ala Gln Glu Tyr Asn Asp Tyr Lys Phe Asp His Ser Lys Asn Pro
65                  70                  75                  80
Ser Val Gly Thr Tyr Val Ser Ile Leu Phe Gly Thr Arg Ile Val Val
                85                  90                  95
Thr Lys Asp Pro Glu Asn Ile Lys Ala Ile Leu Ala Thr Gln Phe Gly
            100                 105                 110
Asp Phe Ser Leu Gly Lys Arg His Thr Leu Phe Lys Pro Leu Leu Gly
        115                 120                 125
Asp Gly Ile Phe Thr Leu Asp Gly Glu Gly Trp Lys His Ser Arg Ala
    130                 135                 140
Met Leu Arg Pro Gln Phe Ala Arg Glu Gln Val Ala His Val Thr Ser
145                 150                 155                 160
Leu Glu Pro His Phe Gln Leu Leu Lys Lys His Ile Leu Lys His Lys
                165                 170                 175
Gly Glu Tyr Phe Asp Ile Gln Glu Leu Phe Phe Arg Phe Thr Val Asp
            180                 185                 190
Ser Ala Thr Glu Phe Leu Phe Gly Glu Ser Val His Ser Leu Lys Asp
        195                 200                 205
Glu Ser Ile Gly Ile Asn Gln Asp Asp Ile Asp Phe Ala Gly Arg Lys
    210                 215                 220
Asp Phe Ala Glu Ser Phe Asn Lys Ala Gln Glu Tyr Leu Ala Ile Arg
225                 230                 235                 240
Thr Leu Val Gln Thr Phe Tyr Trp Leu Val Asn Asn Lys Glu Phe Arg
                245                 250                 255
Asp Cys Thr Lys Leu Val His Lys Phe Thr Asn Tyr Tyr Val Gln Lys
            260                 265                 270
Ala Leu Asp Ala Ser Pro Glu Glu Leu Glu Lys Gln Ser Gly Tyr Val
        275                 280                 285
Phe Leu Tyr Glu Leu Val Lys Gln Thr Arg Asp Pro Asn Val Leu Arg
    290                 295                 300
Asp Gln Ser Leu Asn Ile Leu Leu Ala Gly Arg Asp Thr Thr Ala Gly
305                 310                 315                 320
Leu Leu Ser Phe Ala Val Phe Glu Leu Ala Arg His Pro Glu Ile Trp
                325                 330                 335
Ala Lys Leu Arg Glu Glu Ile Glu Gln Gln Phe Gly Leu Gly Glu Asp
            340                 345                 350
Ser Arg Val Glu Glu Ile Thr Phe Glu Ser Leu Lys Arg Cys Glu Tyr
        355                 360                 365
Leu Lys Ala Phe Leu Asn Glu Thr Leu Arg Ile Tyr Pro Ser Val Pro
    370                 375                 380
Arg Asn Phe Arg Ile Ala Thr Lys Asn Thr Thr Leu Pro Arg Gly Gly
385                 390                 395                 400
Gly Ser Asp Gly Thr Ser Pro Ile Leu Ile Gln Lys Gly Glu Ala Val
                405                 410                 415
Ser Tyr Gly Ile Asn Ser Thr His Leu Asp Pro Val Tyr Tyr Gly Pro
            420                 425                 430
Asp Ala Ala Glu Phe Arg Pro Glu Arg Trp Phe Glu Pro Ser Thr Lys
        435                 440                 445
Lys Leu Gly Trp Ala Tyr Leu Pro Phe Asn Gly Gly Pro Arg Ile Cys
    450                 455                 460
Leu Gly Gln Gln Phe Ala Leu Thr Glu Ala Gly Tyr Val Leu Val Arg
465                 470                 475                 480
Leu Val Gln Glu Phe Ser His Val Arg Leu Asp Pro Asp Glu Val Tyr
                485                 490                 495
```

```
Pro Pro Lys Arg Leu Thr Asn Leu Thr Met Cys Leu Gln Asp Gly Ala
                500                 505                 510
Ile Val Lys Phe Asp
        515
```

(2) INFORMATION FOR SEQ ID NO:101:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 517 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

```
Met Ile Glu Gln Ile Leu Glu Tyr Trp Tyr Ile Val Val Pro Val Leu
1               5                  10                  15
Tyr Ile Ile Lys Gln Leu Ile Ala Tyr Ser Lys Thr Arg Val Leu Met
            20                  25                  30
Lys Gln Leu Gly Ala Ala Pro Ile Thr Asn Gln Leu Tyr Asp Asn Val
        35                  40                  45
Phe Gly Ile Val Asn Gly Trp Lys Ala Leu Gln Phe Lys Lys Glu Gly
    50                  55                  60
Arg Ala Gln Glu Tyr Asn Asp His Lys Phe Asp Ser Ser Lys Asn Pro
65                  70                  75                  80
Ser Val Gly Thr Tyr Val Ser Ile Leu Phe Gly Thr Lys Ile Val Val
                85                  90                  95
Thr Lys Asp Pro Glu Asn Ile Lys Ala Ile Leu Ala Thr Gln Phe Gly
            100                 105                 110
Asp Phe Ser Leu Gly Lys Arg His Ala Leu Phe Lys Pro Leu Leu Gly
        115                 120                 125
Asp Gly Ile Phe Thr Leu Asp Gly Glu Gly Trp Lys His Ser Arg Ser
    130                 135                 140
Met Leu Arg Pro Gln Phe Ala Arg Glu Gln Val Ala His Val Thr Ser
145                 150                 155                 160
Leu Glu Pro His Phe Gln Leu Leu Lys Lys His Ile Leu Lys His Lys
                165                 170                 175
Gly Glu Tyr Phe Asp Ile Gln Glu Leu Phe Phe Arg Phe Thr Val Asp
            180                 185                 190
Ser Ala Thr Glu Phe Leu Phe Gly Glu Ser Val His Ser Leu Lys Asp
        195                 200                 205
Glu Thr Ile Gly Ile Asn Gln Asp Asp Ile Asp Phe Ala Gly Arg Lys
    210                 215                 220
Asp Phe Ala Glu Ser Phe Asn Lys Ala Gln Glu Tyr Leu Ser Ile Arg
225                 230                 235                 240
Ile Leu Val Gln Thr Phe Tyr Trp Leu Ile Asn Asn Lys Glu Phe Arg
                245                 250                 255
Asp Cys Thr Lys Leu Val His Lys Phe Thr Asn Tyr Tyr Val Gln Lys
            260                 265                 270
Ala Leu Asp Ala Thr Pro Glu Glu Leu Glu Lys Gln Gly Gly Tyr Val
        275                 280                 285
Phe Leu Tyr Glu Leu Val Lys Gln Thr Arg Asp Pro Lys Val Leu Arg
    290                 295                 300
Asp Gln Ser Leu Asn Ile Leu Leu Ala Gly Arg Asp Thr Thr Ala Gly
305                 310                 315                 320
Leu Leu Ser Phe Ala Val Phe Glu Leu Ala Arg Asn Pro His Ile Trp
                325                 330                 335
```

Ala Lys Leu Arg Glu Glu Il Glu Gln Gln Phe Gly Leu Gly Glu Asp
340 345 350
Ser Arg Val Glu Glu Ile Thr Phe Glu Ser Leu Lys Arg Cys Glu Tyr
355 360 365
Leu Lys Ala Phe Leu Asn Glu Thr Leu Arg Val Tyr Pro Ser Val Pro
370 375 380
Arg Asn Phe Arg Ile Ala Thr Lys Asn Thr Thr Leu Pro Arg Gly Gly
385 390 395 400
Gly Pro Asp Gly Thr Gln Pro Ile Leu Ile Gln Lys Gly Glu Gly Val
405 410 415
Ser Tyr Gly Ile Asn Ser Thr His Leu Asp Pro Val Tyr Tyr Gly Pro
420 425 430
Asp Ala Ala Glu Phe Arg Pro Glu Arg Trp Phe Glu Pro Ser Thr Arg
435 440 445
Lys Leu Gly Trp Ala Tyr Leu Pro Phe Asn Gly Gly Pro Arg Ile Cys
450 455 460
Leu Gly Gln Gln Phe Ala Leu Thr Glu Ala Gly Tyr Val Leu Val Arg
465 470 475 480
Leu Val Gln Glu Phe Ser His Ile Arg Leu Asp Pro Asp Glu Val Tyr
485 490 495
Pro Pro Lys Arg Leu Thr Asn Leu Thr Met Cys Leu Gln Asp Gly Ala
500 505 510
Ile Val Lys Phe Asp
515

(2) INFORMATION FOR SEQ ID NO:102:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 512 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: unknown
(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:
Met Leu Asp Gln Ile Leu His Tyr Trp Tyr Ile Val Leu Pro Leu Leu
1 5 10 15
Ala Ile Ile Asn Gln Ile Val Ala His Val Arg Thr Asn Tyr Leu Met
20 25 30
Lys Lys Leu Gly Ala Lys Pro Phe Thr His Val Gln Arg Asp Gly Trp
35 40 45
Leu Gly Phe Lys Phe Gly Arg Glu Phe Leu Lys Ala Lys Ser Ala Gly
50 55 60
Arg Leu Val Asp Leu Ile Ile Ser Arg Phe His Asp Asn Glu Asp Thr
65 70 75 80
Phe Ser Ser Tyr Ala Phe Gly Asn His Val Val Phe Thr Arg Asp Pro
85 90 95
Glu Asn Ile Lys Ala Leu Leu Ala Thr Gln Phe Gly Asp Phe Ser Leu
100 105 110
Gly Ser Arg Val Lys Phe Phe Lys Pro Leu Leu Gly Tyr Gly Ile Phe
115 120 125
Thr Leu Asp Ala Glu Gly Trp Lys His Ser Arg Ala Met Leu Arg Pro
130 135 140
Gln Phe Ala Arg Glu Gln Val Ala His Val Thr Ser Leu Glu Pro His
145 150 155 160
Phe Gln Leu Leu Lys Lys His Ile Leu Lys His Lys Gly Glu Tyr Phe
165 170 175

```
Asp Ile Gln Glu Leu Phe Phe Arg Phe Thr Val Asp Ser Ala Thr Glu
            180                 185                 190
Phe Leu Phe Gly Glu Ser Val His Ser Leu Lys Asp Glu Glu Ile Gly
        195                 200                 205
Tyr Asp Thr Lys Asp Met Ser Glu Glu Arg Arg Arg Phe Ala Asp Ala
    210                 215                 220

Phe Asn Lys Ser Gln Val Tyr Val Ala Thr Arg Val Ala Leu Gln Asn
225                 230                 235                 240
Leu Tyr Trp Leu Val Asn Asn Lys Glu Phe Lys Glu Cys Asn Asp Ile
                245                 250                 255
Val His Lys Phe Thr Asn Tyr Tyr Val Gln Lys Ala Leu Asp Ala Thr
            260                 265                 270
Pro Glu Glu Leu Glu Lys Gln Gly Gly Tyr Val Phe Leu Tyr Glu Leu
        275                 280                 285
Val Lys Gln Thr Arg Asp Pro Lys Val Leu Arg Asp Gln Ser Leu Asn
    290                 295                 300
Ile Leu Leu Ala Gly Arg Asp Thr Thr Ala Gly Leu Leu Ser Phe Ala
305                 310                 315                 320
Val Phe Glu Leu Ala Arg Asn Pro His Ile Trp Ala Lys Leu Arg Glu
                325                 330                 335
Glu Ile Glu Gln Gln Phe Gly Leu Gly Glu Asp Ser Arg Val Glu Glu
            340                 345                 350
Ile Thr Phe Glu Ser Leu Lys Arg Cys Glu Tyr Leu Lys Ala Val Leu
        355                 360                 365
Asn Glu Thr Leu Arg Leu His Pro Ser Val Pro Arg Asn Ala Arg Phe
    370                 375                 380
Ala Ile Lys Asp Thr Thr Leu Pro Arg Gly Gly Gly Pro Asn Gly Lys
385                 390                 395                 400
Asp Pro Ile Leu Ile Arg Lys Asp Glu Val Val Gln Tyr Ser Ile Ser
                405                 410                 415
Ala Thr Gln Thr Asn Pro Ala Tyr Tyr Gly Ala Asp Ala Ala Asp Phe
            420                 425                 430
Arg Pro Glu Arg Trp Phe Glu Pro Ser Thr Arg Asn Leu Gly Trp Ala
        435                 440                 445
Phe Leu Pro Phe Asn Gly Gly Pro Arg Ile Cys Leu Gly Gln Gln Phe
    450                 455                 460
Ala Leu Thr Glu Ala Gly Tyr Val Leu Val Arg Leu Val Gln Glu Phe
465                 470                 475                 480
Pro Asn Leu Ser Gln Asp Pro Glu Thr Lys Tyr Pro Pro Pro Arg Leu
                485                 490                 495
Ala His Leu Thr Met Cys Leu Phe Asp Gly Ala His Val Lys Met Ser
            500                 505                 510
```

(2) INFORMATION FOR SEQ ID NO:103:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 512 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

```
Met Leu Asp Gln Ile Phe His Tyr Trp Tyr Ile Val Leu Pro Leu Leu
1               5                   10                  15
Val Ile Ile Lys Gln Ile Val Ala His Ala Arg Thr Asn Tyr Leu Met
            20                  25                  30
```

```
Lys Lys Leu Gly Ala Lys Pro Phe Thr His Val Gln Leu Asp Gly Trp
        35                  40                  45
Phe Gly Phe Lys Phe Gly Arg Glu Phe Leu Lys Ala Lys Ser Ala Gly
    50                  55                  60
Arg Gln Val Asp Leu Ile Ile Ser Arg Phe His Asp Asn Glu Asp Thr
65                  70                  75                  80
Phe Ser Ser Tyr Ala Phe Gly Asn His Val Val Phe Thr Arg Asp Pro
                85                  90                  95
Glu Asn Ile Lys Ala Leu Leu Ala Thr Gln Phe Gly Asp Phe Ser Leu
            100                 105                 110
Gly Ser Arg Val Lys Phe Phe Lys Pro Leu Leu Gly Tyr Gly Ile Phe
        115                 120                 125
Thr Leu Asp Gly Glu Gly Trp Lys His Ser Arg Ala Met Leu Arg Pro
    130                 135                 140
Gln Phe Ala Arg Glu Gln Val Ala His Val Thr Ser Leu Glu Pro His
145                 150                 155                 160
Phe Gln Leu Leu Lys Lys His Ile Leu Lys His Lys Gly Glu Tyr Phe
                165                 170                 175
Asp Ile Gln Glu Leu Phe Phe Arg Phe Thr Val Asp Ser Ala Thr Glu
            180                 185                 190
Phe Leu Phe Gly Glu Ser Val His Ser Leu Arg Asp Glu Glu Ile Gly
        195                 200                 205
Tyr Asp Thr Lys Asp Met Ala Glu Glu Arg Arg Lys Phe Ala Asp Ala
    210                 215                 220
Phe Asn Lys Ser Gln Val Tyr Leu Ser Thr Arg Val Ala Leu Gln Thr
225                 230                 235                 240
Leu Tyr Trp Leu Val Asn Asn Lys Glu Phe Lys Glu Cys Asn Asp Ile
                245                 250                 255
Val His Lys Phe Thr Asn Tyr Tyr Val Gln Lys Ala Leu Asp Ala Thr
            260                 265                 270
Pro Glu Glu Leu Glu Lys Gln Gly Gly Tyr Val Phe Leu Tyr Glu Leu
        275                 280                 285
Ala Lys Gln Thr Lys Asp Pro Asn Val Leu Arg Asp Gln Ser Leu Asn
    290                 295                 300
Ile Leu Leu Ala Gly Arg Asp Thr Thr Ala Gly Leu Leu Ser Phe Ala
305                 310                 315                 320
Val Phe Glu Leu Ala Arg Asn Pro His Ile Trp Ala Lys Leu Arg Glu
                325                 330                 335
Glu Ile Glu Ser His Phe Gly Leu Gly Glu Asp Ser Arg Val Glu Glu
            340                 345                 350
Ile Thr Phe Glu Ser Leu Lys Arg Cys Glu Tyr Leu Lys Ala Val Leu
        355                 360                 365
Asn Glu Thr Leu Arg Leu His Pro Ser Val Pro Arg Asn Ala Arg Phe
    370                 375                 380
Ala Ile Lys Asp Thr Thr Leu Pro Arg Gly Gly Gly Pro Asn Gly Lys
385                 390                 395                 400
Asp Pro Ile Leu Ile Arg Lys Asn Glu Val Val Gln Tyr Ser Ile Ser
                405                 410                 415
Ala Thr Gln Thr Asn Pro Ala Tyr Tyr Gly Ala Asp Ala Ala Asp Phe
            420                 425                 430
Arg Pro Glu Arg Trp Phe Glu Pro Ser Thr Arg Asn Leu Gly Trp Ala
        435                 440                 445
Tyr Leu Pro Phe Asn Gly Gly Pro Arg Ile Cys Leu Gly Gln Gln Phe
    450                 455                 460
Ala Leu Thr Glu Ala Gly Tyr Val Leu Val Arg Leu Val Gln Glu Phe
465                 470                 475                 480
```

```
Pro Ser Leu Ser Gln Asp Pro Glu Thr Glu Tyr Pro Pro Pro Arg Leu
                485                 490                 495
Ala His Leu Thr Met Cys Leu Phe Asp Gly Ala Tyr Val Lys Met Gln
            500                 505                 510
```

(2) INFORMATION FOR SEQ ID NO:104:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 499 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

```
Met Ala Ile Ser Ser Leu Leu Ser Trp Asp Val Ile Cys Val Val Phe
1               5                   10                  15
Ile Cys Val Cys Val Tyr Phe Gly Tyr Glu Tyr Cys Tyr Thr Lys Tyr
            20                  25                  30
Leu Met His Lys His Gly Ala Arg Glu Ile Glu Asn Val Ile Asn Asp
        35                  40                  45
Gly Phe Phe Gly Phe Arg Leu Pro Leu Leu Leu Met Arg Ala Ser Asn
    50                  55                  60
Glu Gly Arg Leu Ile Glu Phe Ser Val Lys Arg Phe Glu Ser Ala Pro
65                  70                  75                  80
His Pro Gln Asn Lys Thr Leu Val Asn Arg Ala Leu Ser Val Pro Val
                85                  90                  95
Ile Leu Thr Lys Asp Pro Val Asn Ile Lys Ala Met Leu Ser Thr Gln
            100                 105                 110
Phe Asp Asp Phe Ser Leu Gly Leu Arg Leu His Gln Phe Ala Pro Leu
        115                 120                 125
Leu Gly Lys Gly Ile Phe Thr Leu Asp Gly Pro Glu Trp Lys Gln Ser
    130                 135                 140
Arg Ser Met Leu Arg Pro Gln Phe Ala Lys Asp Arg Val Ser His Ile
145                 150                 155                 160
Leu Asp Leu Glu Pro His Phe Val Leu Leu Arg Lys His Ile Asp Gly
                165                 170                 175
His Asn Gly Asp Tyr Phe Asp Ile Gln Glu Leu Tyr Phe Arg Phe Ser
            180                 185                 190
Met Asp Val Ala Thr Gly Phe Leu Phe Gly Glu Ser Val Gly Ser Leu
        195                 200                 205
Lys Asp Glu Asp Ala Arg Phe Leu Glu Ala Phe Asn Glu Ser Gln Lys
    210                 215                 220
Tyr Leu Ala Thr Arg Ala Thr Leu His Glu Leu Tyr Phe Leu Cys Asp
225                 230                 235                 240
Gly Phe Arg Phe Arg Gln Tyr Asn Lys Val Val Arg Lys Phe Cys Ser
                245                 250                 255
Gln Cys Val His Lys Ala Leu Asp Val Ala Pro Glu Asp Thr Ser Glu
            260                 265                 270
Tyr Val Phe Leu Arg Glu Leu Val Lys His Thr Arg Asp Pro Val Val
        275                 280                 285
Leu Gln Asp Gln Ala Leu Asn Val Leu Leu Ala Gly Arg Asp Thr Thr
    290                 295                 300
Ala Ser Leu Leu Ser Phe Ala Thr Phe Glu Leu Ala Arg Asn Asp His
305                 310                 315                 320
Met Trp Arg Lys Leu Arg Glu Glu Val Ile Leu Thr Met Gly Pro Ser
                325                 330                 335
```

```
Ser Asp Glu Ile Thr Val Ala Gly Leu Lys Ser Cys Arg Tyr Leu Lys
            340                 345                 350
Ala Ile Leu Asn Glu Thr Leu Arg Leu Tyr Pro Ser Val Pro Arg Asn
        355                 360                 365
Ala Arg Phe Ala Thr Arg Asn Thr Thr Leu Pro Arg Gly Gly Gly Pro
    370                 375                 380
Asp Gly Ser Phe Pro Ile Leu Ile Arg Lys Gly Gln Pro Val Gly Tyr
385                 390                 395                 400
Phe Ile Cys Ala Thr His Leu Asn Glu Lys Val Tyr Gly Asn Asp Ser
                405                 410                 415
His Val Phe Arg Pro Glu Arg Trp Ala Ala Leu Glu Gly Lys Ser Leu
            420                 425                 430
Gly Trp Ser Tyr Leu Pro Phe Asn Gly Gly Pro Arg Ser Cys Leu Gly
        435                 440                 445
Gln Gln Phe Ala Ile Leu Glu Ala Ser Tyr Val Leu Ala Arg Leu Thr
    450                 455                 460
Gln Cys Tyr Thr Thr Ile Gln Leu Arg Thr Thr Glu Tyr Pro Pro Lys
465                 470                 475                 480
Lys Leu Val His Leu Thr Met Ser Leu Leu Asn Gly Val Tyr Ile Arg
                485                 490                 495
Thr Arg Thr
```

(2) INFORMATION FOR SEQ ID NO:105:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1712 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

```
GGTACCGAGC TCACGAGTTT TGGGATTTTC GAGTTTGGAT TGTTTCCTTT GTTGATTGAA      60
TTGACGAAAC CAGAGGTTTT CAAGACAGAT AAGATTGGGT TTATCAAAAC GCAGTTTGAA     120
ATATTCCAGT TGGTTTCCAA GATATCTTGA AGAAGATTGA CGATTTGAAA TTTGAAGAAG     180
TGGAGAAGAT CTGGTTTGGA TTGTTGGAGA ATTTCAAGAA TCTCAAGATT TACTCTAACG     240
ACGGGTACAA CGAGAATTGT ATTGAATTGA TCAAGAACAT GATCTTGGTG TTACAGAACA     300
TCAAGTTCTT GGACCAGACT GAGAATGCCA CAGATATACA AGGCGTCATG TGATAAAATG     360
GATGAGATTT ATCCCACAAT TGAAGAAAGA GTTTATGGAA AGTGGTCAAC CAGAAGCTAA     420
ACAGGAAGAA GCAAACGAAG AGGTGAAACA AGAAGAAGAA GGTAAATAAG TATTTTGTAT     480
TATATAACAA ACAAAGTAAG GAATACAGAT TTATACAATA AATTGCCATA CTAGTCACGT     540
GAGATATCTC ATCCATTCCC CAACTCCCAA GAAAAAAAAA AAGTGAAAAA AAAAATCAAA     600
CCCAAAGATC AACCTCCCCA TCATCATCGT CATCAAACCC CCAGCTCAAT TCGCAATGGT     660
TAGCACAAAA ACATACACAG AAAGGGCATC AGCACACCCC TCCAAGGTTG CCCAACGTTT     720
ATTCCGCTTA ATGGAGTCCA AAAAGACCAA CCTCTGCGCC TCGATCGACG TGACCACAAC     780
CGCCGAGTTC CTTTCGCTCA TCGACAAGCT CGGTCCCCAC ATCTGTCTCG TGAAGACGCA     840
CATCGATATC ATCTCAGACT TCAGCTACGA GGGCACGATT GAGCCGTTGC TTGTGCTTGC     900
AGAGCGCCAC GGGTTCTTGA TATTCGAGGA CAGGAAGTTT GCTGATATCG GAAACACCGT     960
GATGTTGCAG TACACCTCGG GGGTATACCG GATCGCGGCG TGGAGTGACA TCACGAACGC    1020
GCACGGAGTG ACTGGGAAGG GCGTCGTTGA AGGGTTGAAA CGCGGTGCGG AGGGGGTAGA    1080
AAAGGAAAGG GGCGTGTTGA TGTTGGCGGA GTTGTCGAGT AAAGGCTCGT TGGCGCATGG    1140
TGAATATACC CGTGAGACGA TCGAGATTGC GAAGAGTGAT CGGGAGTTCG TGATTGGGTT    1200
CATCGCGCAG CGGGACATGG GGGGTAGAGA AGAAGGGTTT GATTGGATCA TCATGACGCC    1260
TGGTGTGGGG TTGGATGATA AAGGCGATGC GTTGGGCCAG CAGTATAGGA CTGTTGATGA    1320
GGTGGTTCTG ACTGGTACCG ATGTGATTAT TGTCGGGAGA GGGTTGTTTG GAAAAGGAAG    1380
AGACCCTGAG GTGGAGGGAA AGAGATACAG GGATGCTGGA TGGAAGGCAT ACTTGAAGAG    1440
AACTGGTCAG TTAGAATAAA TATTGTAATA AATAGGTCTA TATACATACA CTAAGCTTCT    1500
AGGACGTCAT TGTAGTCTTC GAAGTTGTCT GCTAGTTTAG TTCTCATGAT TTCGAAAACC    1560
```

AATAACGCAA TGGATGTAGC AGGGATGGTG GTTAGTGCGT TCCTGACAAA CCCAGAGTAC 1620
GCCGCCTCAA ACCACGTCAC ATTCGCCCTT TGCTTCATCC GCATCACTTG CTTGAAGGTA 1680
TCCACGTACG AGTTGTAATA CACCTTGAAG AA 1712

(2) INFORMATION FOR SEQ ID NO:106:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 267 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: unknown
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:

Met Val Ser Thr Lys Thr Tyr Thr Glu Arg Ala Ser Ala His Pro Ser
1 5 10 15
Lys Val Ala Gln Arg Leu Phe Arg Leu Met Glu Ser Lys Lys Thr Asn
20 25 30
Leu Cys Ala Ser Ile Asp Val Thr Thr Thr Ala Glu Phe Leu Ser Leu
35 40 45
Ile Asp Lys Leu Gly Pro His Ile Cys Leu Val Lys Thr His Ile Asp
50 55 60
Ile Ile Ser Asp Phe Ser Tyr Glu Gly Thr Ile Glu Pro Leu Leu Val
65 70 75 80
Leu Ala Glu Arg His Gly Phe Leu Ile Phe Glu Asp Arg Lys Phe Ala
85 90 95
Asp Ile Gly Asn Thr Val Met Leu Gln Tyr Thr Ser Gly Val Tyr Arg
100 105 110
Ile Ala Ala Trp Ser Asp Ile Thr Asn Ala His Gly Val Thr Gly Lys
115 120 125
Gly Val Val Glu Gly Leu Lys Arg Gly Ala Glu Gly Val Glu Lys Glu
130 135 140
Arg Gly Val Leu Met Leu Ala Glu Leu Ser Ser Lys Gly Ser Leu Ala
145 150 155 160
His Gly Glu Tyr Thr Arg Glu Thr Ile Glu Ile Ala Lys Ser Asp Arg
165 170 175
Glu Phe Val Ile Gly Phe Ile Ala Gln Arg Asp Met Gly Gly Arg Glu
180 185 190
Glu Gly Phe Asp Trp Ile Ile Met Thr Pro Gly Val Gly Leu Asp Asp
195 200 205
Lys Gly Asp Ala Leu Gly Gln Gln Tyr Arg Thr Val Asp Glu Val Val
210 215 220
Leu Thr Gly Thr Asp Val Ile Ile Val Gly Arg Gly Leu Phe Gly Lys
225 230 235 240
Gly Arg Asp Pro Glu Val Glu Gly Lys Arg Tyr Arg Asp Ala Gly Trp
245 250 255
Lys Ala Tyr Leu Lys Arg Thr Gly Gln Leu Glu
260 265

(2) INFORMATION FOR SEQ ID NO:107:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 473 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

GTCAAAGCAA ATTGTTGGCC CAAGCAGACT CTTGGACCAC CGTTGAATGG AACATAAGCC 60
CAGCCCAACT TCTTAGTAGA TGGTTCAAAC CATCTTTCTG GTCTGAAGTC GTTAGCGTCC 120
TTACCGTAGT ATTCTTCCAA ACGGTGGGTC TTGTAGACAA CGTAAGCAAC AGTGGAGCCT 180
TTAGGAATGT AGATTGGGTC GGTACCGTTA GCACCACCAC CTCTTGGCAA AGTGGTGTCT 240
CTGGTGGCGG TTCTAAAGTT GACAGGAACA GATGGGTACA TACGCAAGGT TTCGTTAAGG 300
ATAGCCTTCA AGTATTCACA TCTCTTCAAG GCTTCGAAAG TAATTTCTTC AACGCGGGAG 360
TCTTCACCAA CACCAAAGTT AACTTCGATT TCTTCTCTCA ACTTGGACCA CATCTCTGGG 420
TGTCTAGCCA ATTCAAACAA AGCAAAGGAC AACAAACCCG CGGTGGTGTC TCT 473

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:
CCTTAATTAA GAGGTCGTTG GTTGAGTTTT C 31

(2) INFORMATION FOR SEQ ID NO:8:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:
CCTTAATTAA TTGATAATGA CGTTGCGGG 29

(2) INFORMATION FOR SEQ ID NO:9:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 33 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:
AGGCGCGCCG GAGTCCAAAA AGACCAACCT CTG 33

(2) INFORMATION FOR SEQ ID NO:10:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 34 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:
CCTTAATTAA TACGTGGATA CCTTCAAGCA AGTG 34

(2) INFORMATION FOR SEQ ID NO:11:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 35 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:
CCTTAATTAA GCTCACGAGT TTTGGGATTT TCGAG 35

(2) INFORMATION FOR SEQ ID NO:12:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 35 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:
GGGTTTAAAC CGCAGAGGTT GGTCTTTTTG GACTC 35